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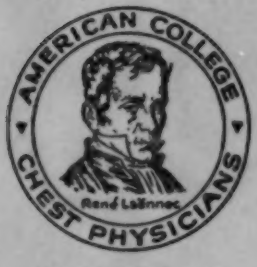
VOLUME XXXII NUMBER 4

DISEASES

of the

CHEST

OFFICIAL PUBLICATION



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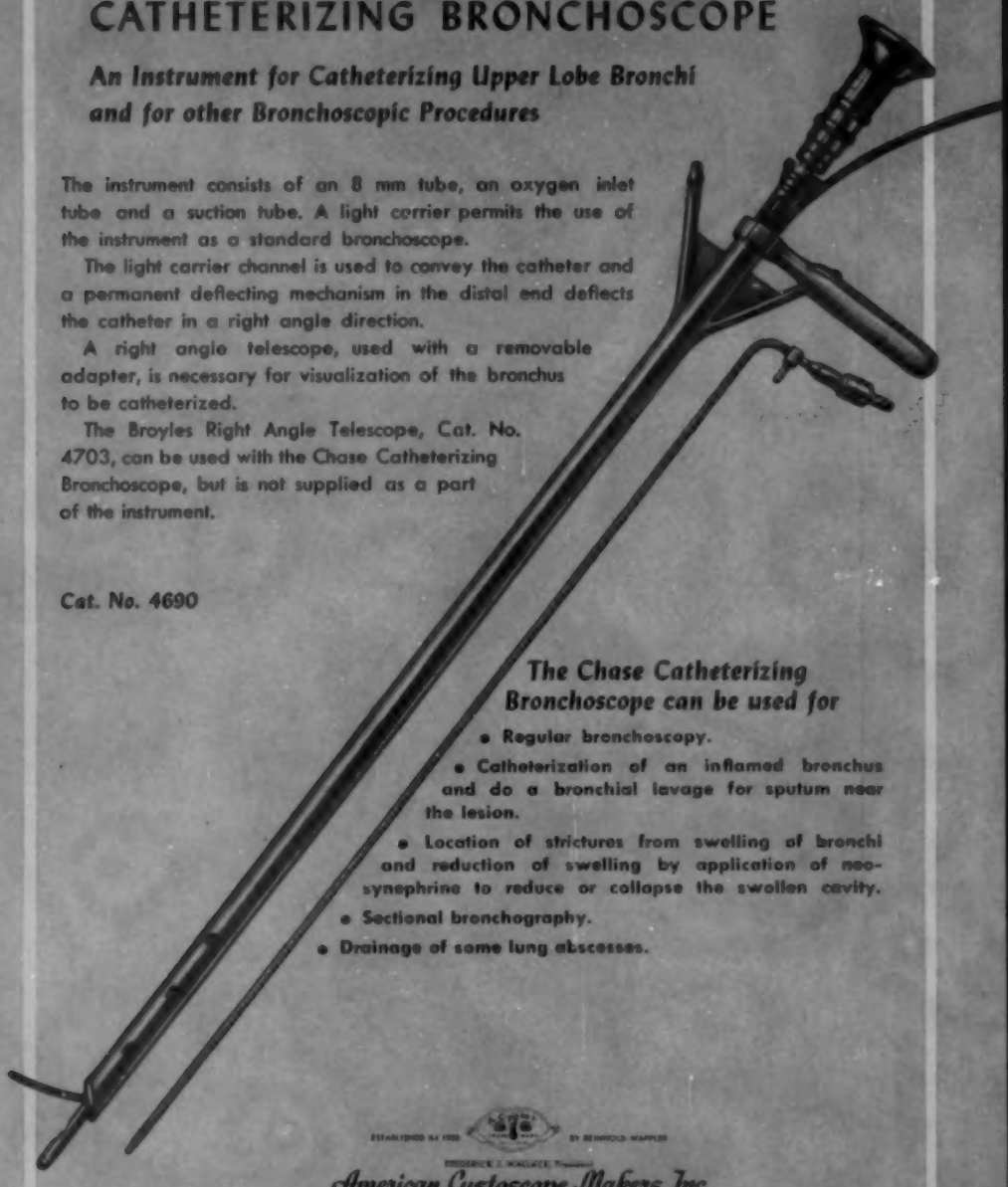

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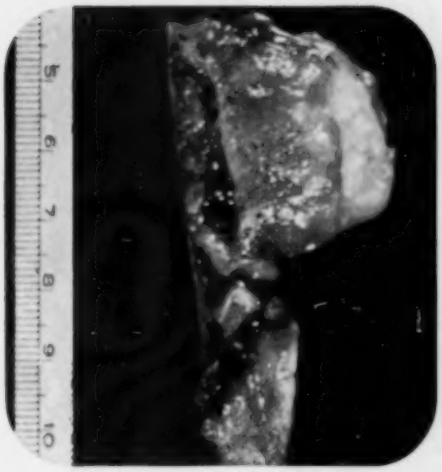

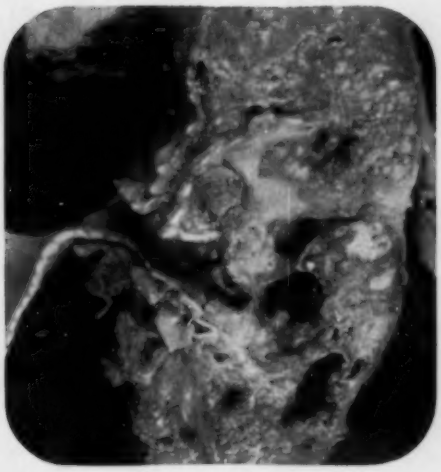

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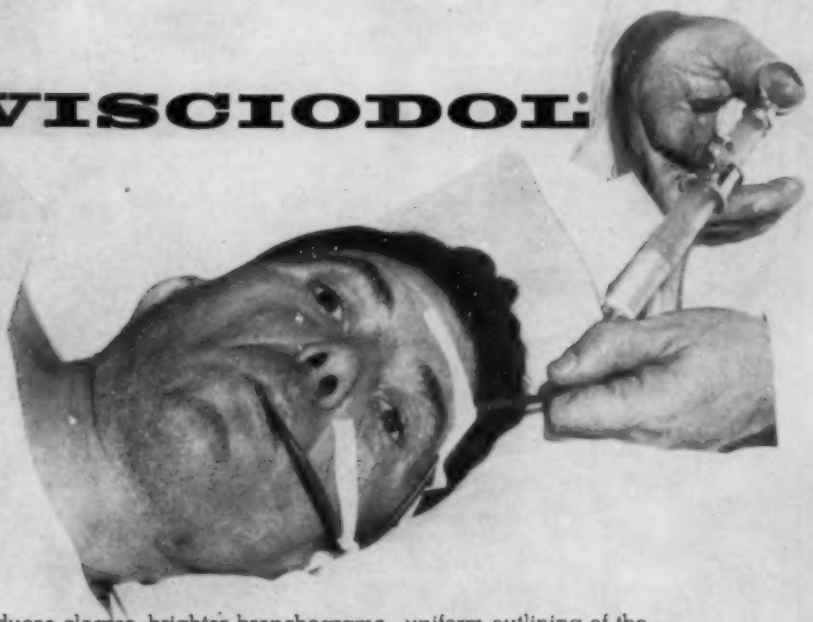

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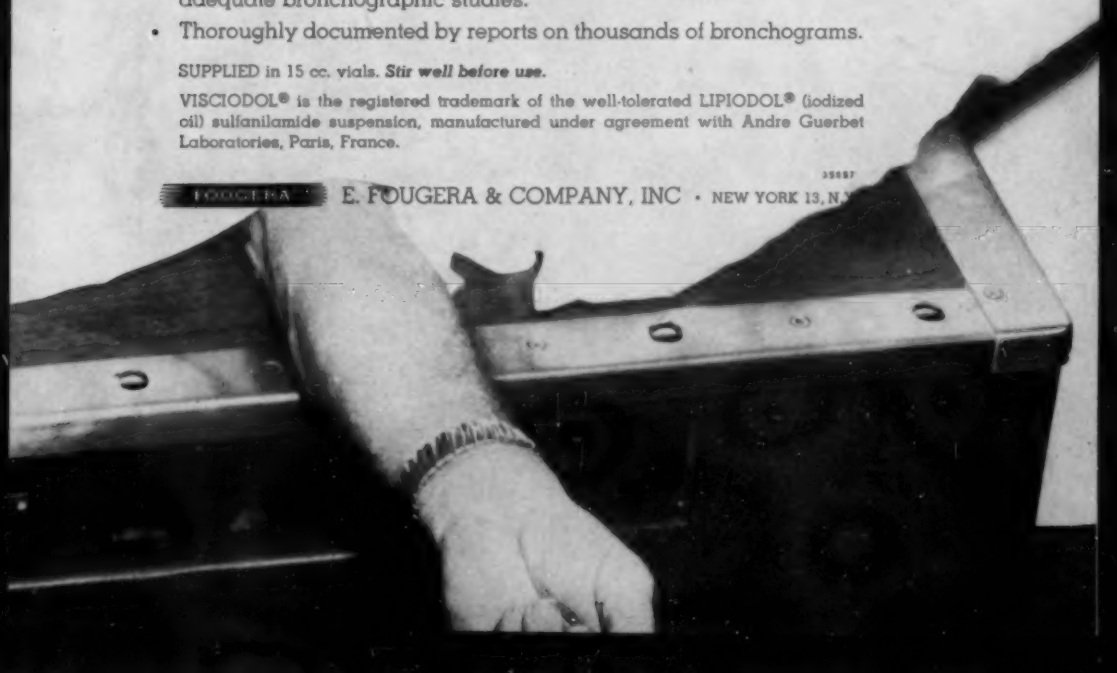

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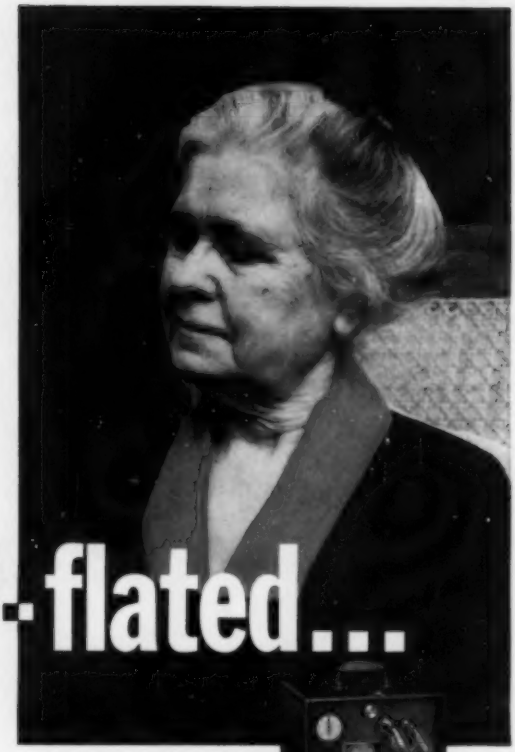

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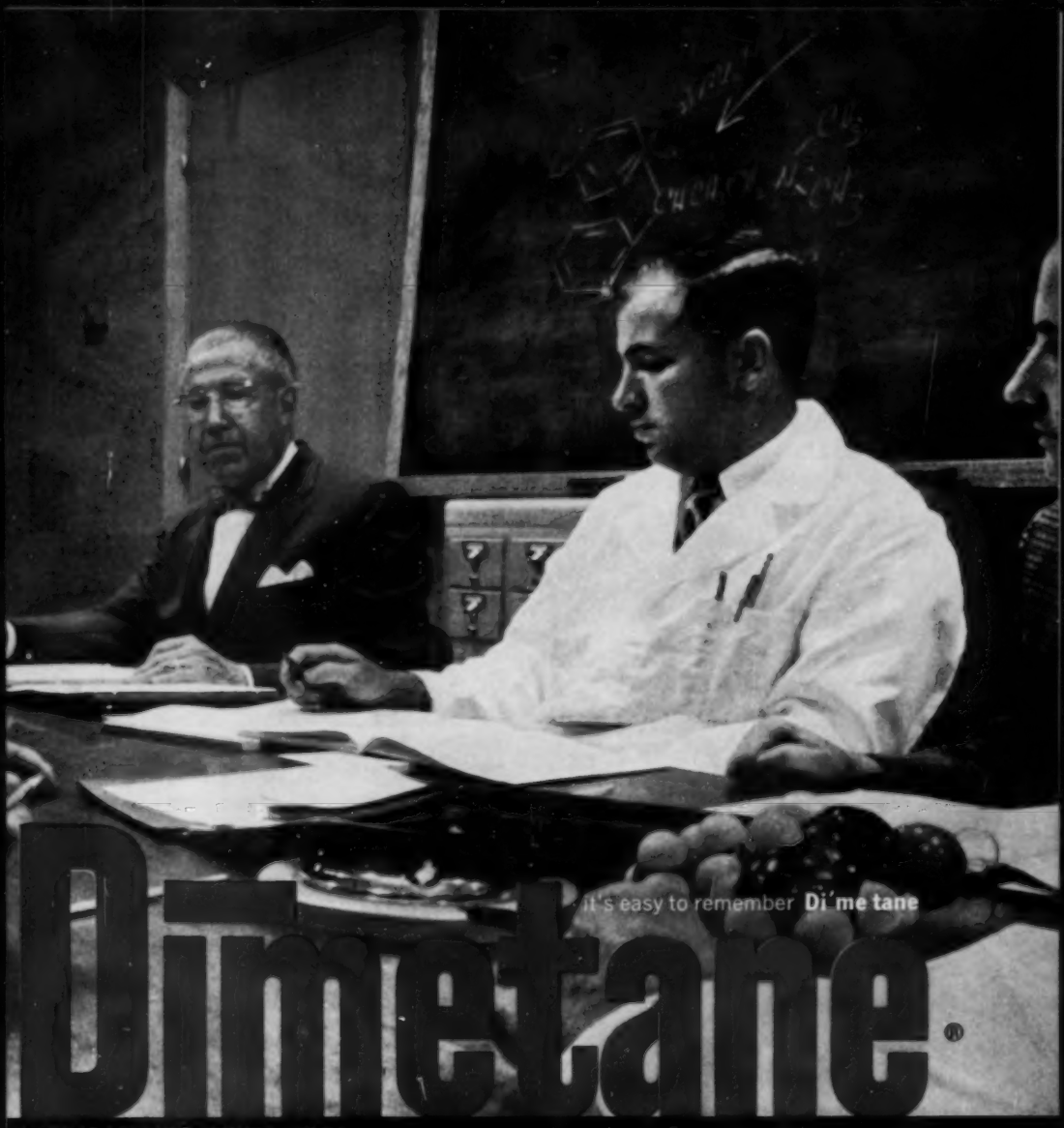

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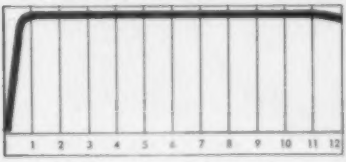

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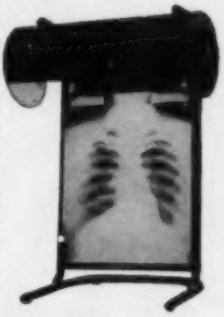

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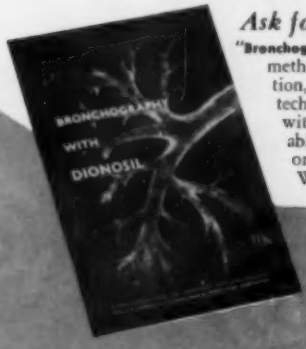

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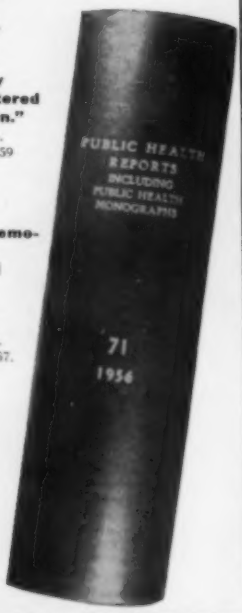
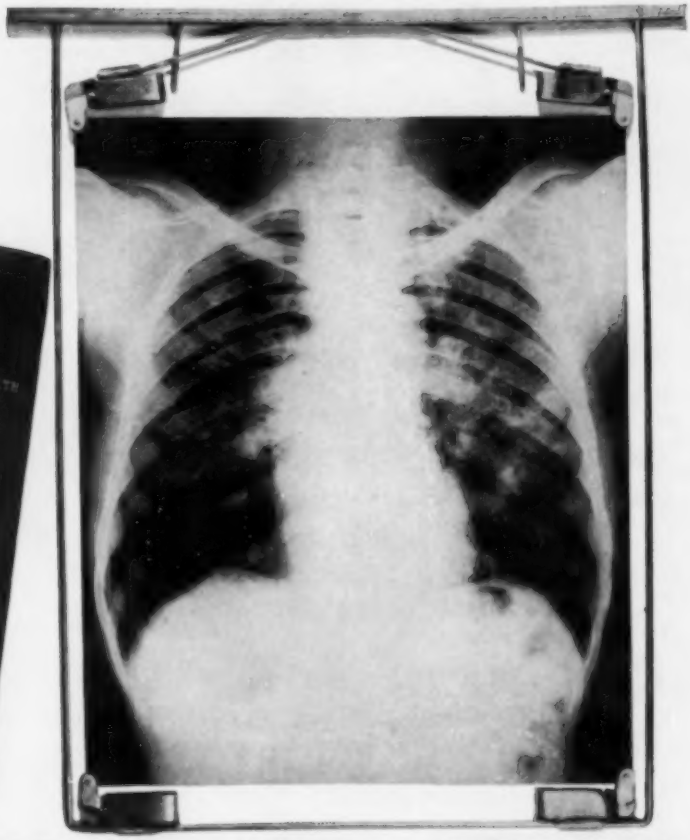
Chapman, P. T.: J. Kentucky M. A. 55:235 (March) 1957.





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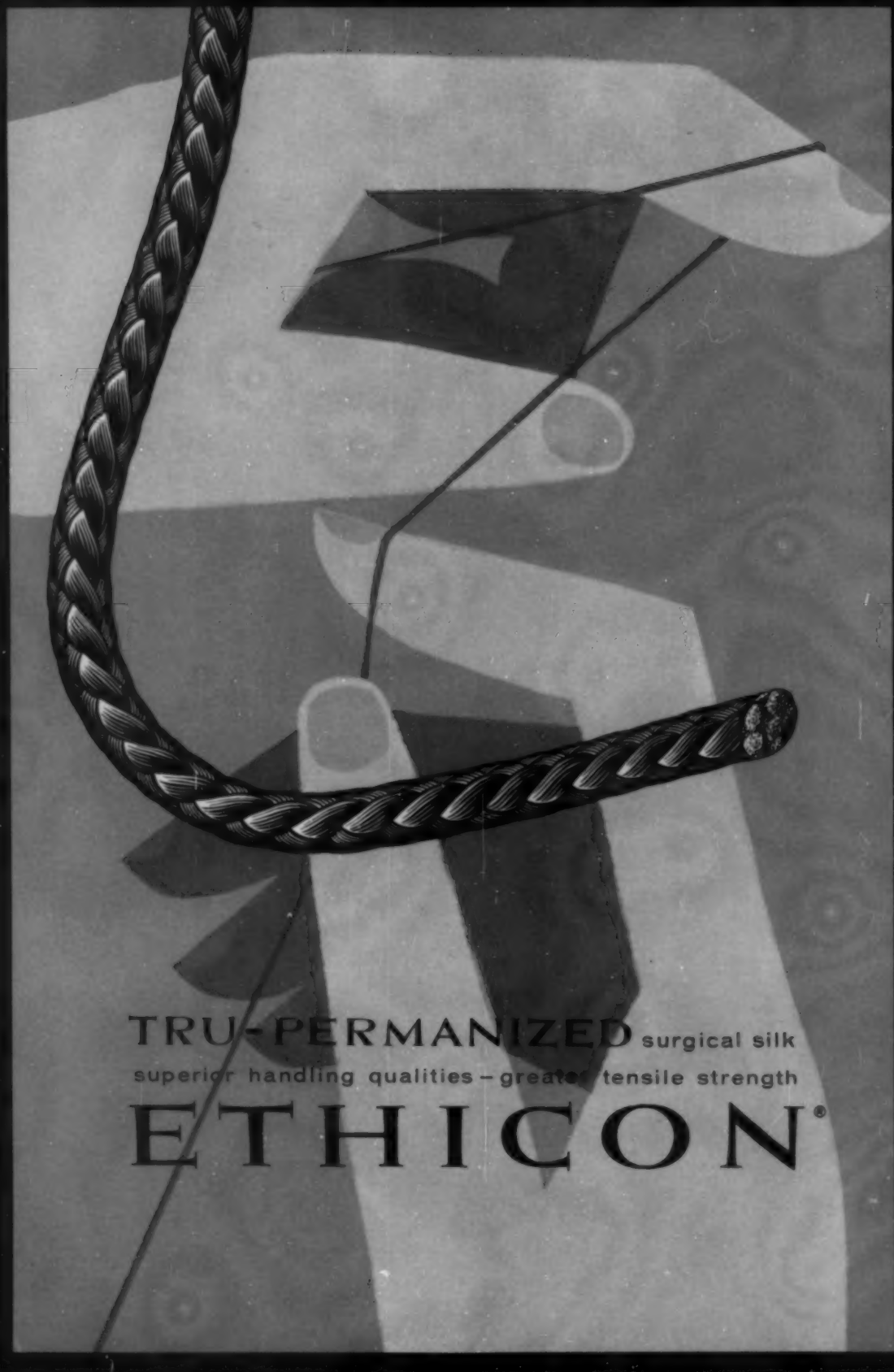
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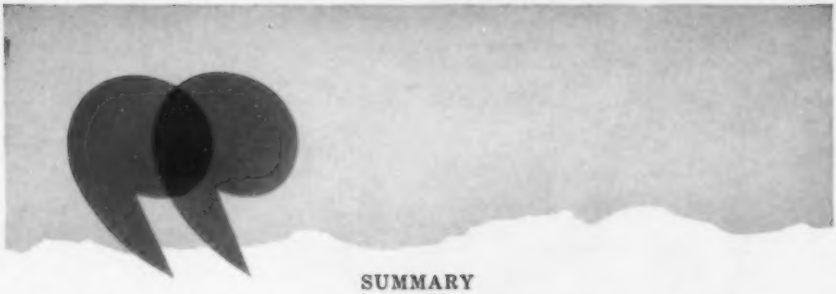


SUMMARY

Potassium para-aminosalicylate (KPAS) was administered to 120 patients with tuberculosis.

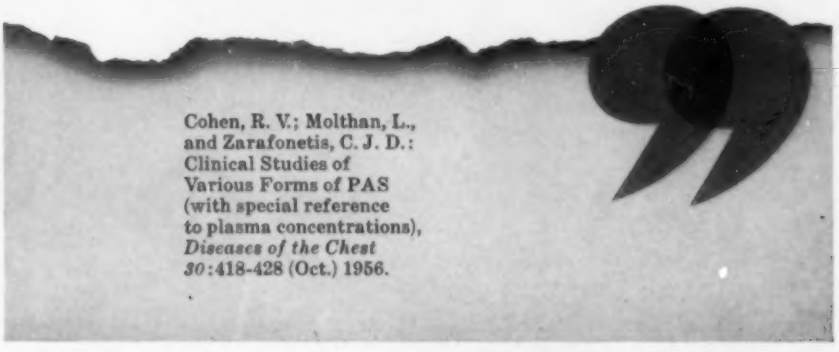
One hundred fifteen (96 per cent) tolerated 12 gm. daily doses of KPAS without difficulty. There were no evidences of potassium toxicity.

Plasma PAS concentration studies revealed that KPAS is more rapidly absorbed and yields significantly higher values than either PAS or NaPAS.

KPAS is ideally suited for use in patients with congestive heart failure, pregnancy, or other situations in which use of the sodium salt is precluded.

The 10 per cent solution of KPAS was used for "desensitizations" of those who had acquired sensitivity reactions to PAS compounds.

It is concluded that KPAS is superior to other forms of PAS.



Cohen, R. V.; Molthan, L., and Zarafonetis, C. J. D.: Clinical Studies of Various Forms of PAS (with special reference to plasma concentrations), *Diseases of the Chest* *30*:418-428 (Oct.) 1956.

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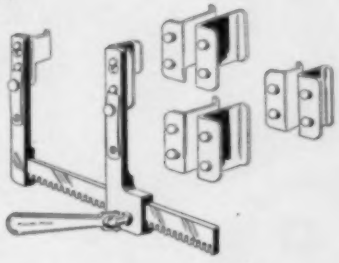

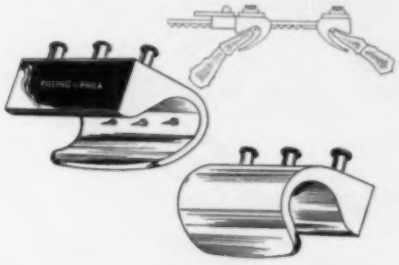

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—*Frequency of Chronic Cor Pulmonale, Especially Among Patients with Stasis Insufficiency:* J.A.M.A. Review; J. Melchior. Ugesk. lager 118:162-166, Feb. 9, 1956.

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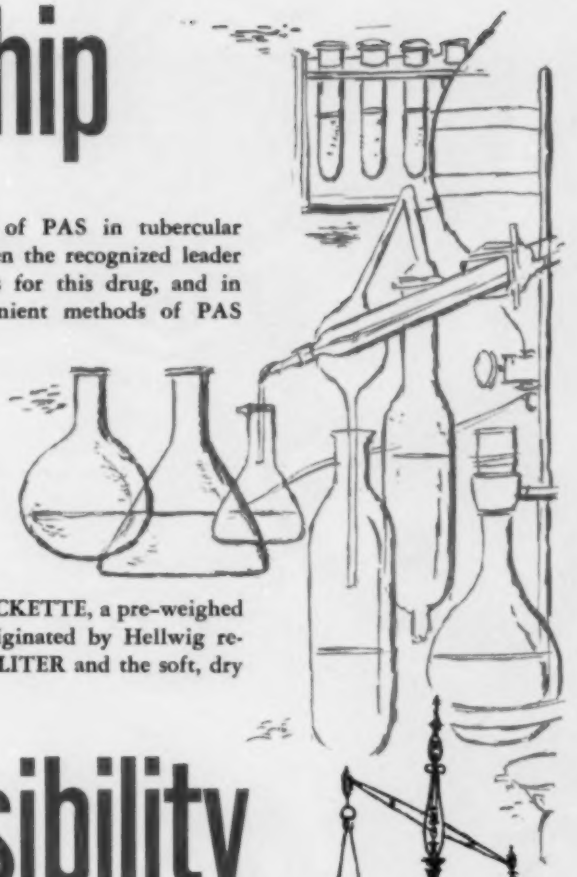

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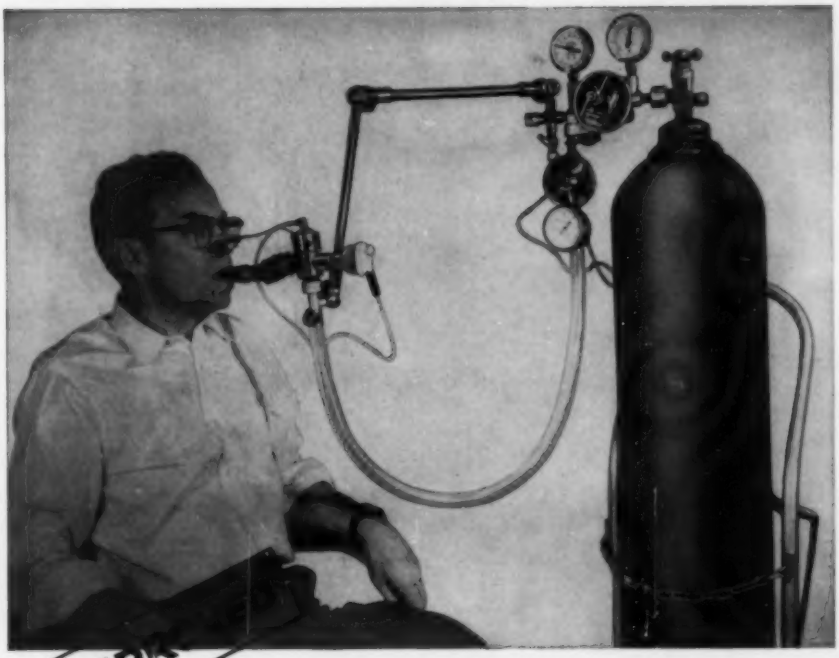

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1. Blanchard, K., and Ford, R. A.: Journal-Lancet 74:443, 1954.
2. Blanchard, K., and Ford R. A.: Rocky Mt. M. J. 52:278, 1955. 3. Cass, L. J., and Frederik, W. S.: Am. Pract. & Dig. Treat. 2:844, 1951.

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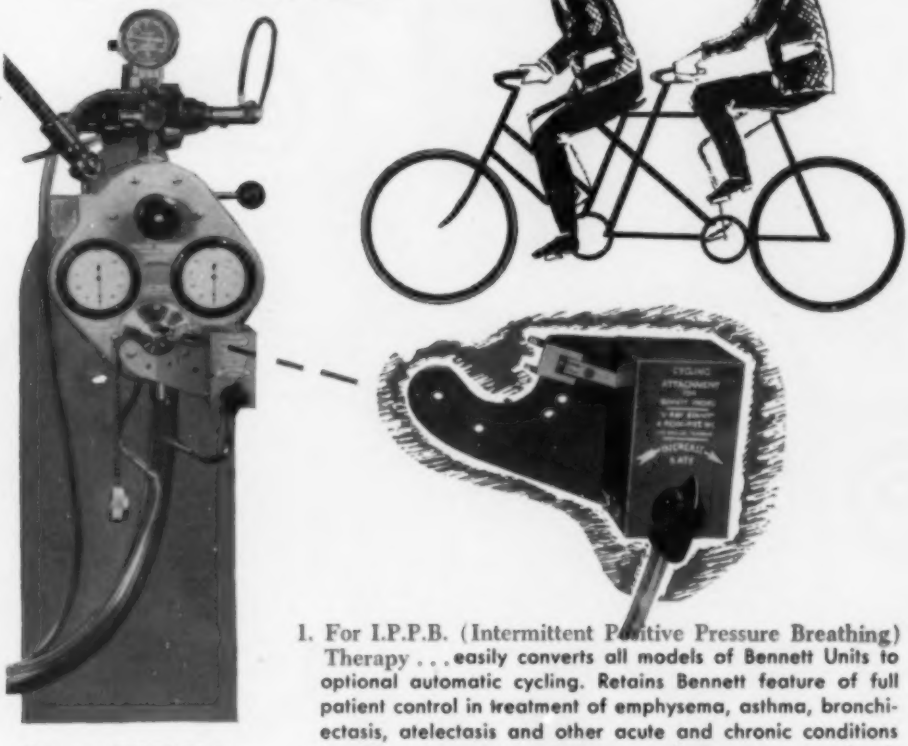

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DISEASES of the CHEST

VOLUME XXXII OCTOBER, 1957 NUMBER 4

Vision in Medicine Today and 65 Years Ago

Introduction

J. ARTHUR MYERS, M.D., F.C.C.P.

Minneapolis, Minnesota

On October 4, 1892, Sir William Osler, Johns Hopkins University, delivered the main address entitled, "Teacher and Student" at the dedication of the first medical building on the campus of the university of Minnesota.

On June 14, 1957, Dr. Paul Dudley White, Harvard University, presented the main address entitled, "The Patient Leads the Way" at the recognition exercises honoring the senior class in medicine.

These physicians reached the top rung of the ladder of achievement so their names were household in medical circles around the world. Because of the contents of their addresses, their positions in world-renowned schools of medicine, and because 65 years elapsed between the two addresses, *Diseases of the Chest* decided to publish Doctor White's paper and reprint that of Doctor Osler in this issue.

During the interval phenomenal changes have occurred in nearly every phase of human activity. In 1892 it required days for Doctor Osler to travel from Baltimore to Minnesota, while in 1957 Doctor White made the trip from Boston in hours. On arrival, Doctor Osler saw one small medical building just completed with a teaching faculty of 29 members. Doctor White saw numerous well-equipped medical buildings with more than 600 faculty members.

Doctor Osler began his address with the following: "Truly it may be said today that in the methods of teaching medicine the old order changeth—." He was in that period known as the glory of the 19th century medicine. Doctor White said, "These are the most exciting days in all history, that of medicine as well as that of the world." He was in that period which probably will always be known as the glory of 20th century medicine. Each of these world-renowned physicians talked from wide experience and made recommendations applicable to those entering the medical profession everywhere in the world.

In 1892 the average length of life in the United States was approximately 35 years. This short span was due in considerable part to highly fatal conditions among children and young adults such as enteritis, pneumonia, typhoid fever, and tuberculosis. It was not unusual for an epidemic of diphtheria to remove from 25 to 50 per cent of the children of a community.

Some acute infections carried over to the upper age brackets. In fact, it was Doctor Osler who said that in some places ". . . . to die of pneumonia is almost the natural end of old people."

Degenerative diseases among older persons were also a serious problem. He spoke of the physical and mental changes that come to people with the years. "It is this loss of mental elasticity which makes men over forty so slow to receive new truths." He said, "There is no sadder picture than the Professor who has outgrown his usefulness, and, the only one unconscious of the fact, insists, with a praiseworthy zeal, upon the performance of duties for which the circumstances of the time have rendered him unfit."

Osler became an eminent diagnostician and therapeutist. He also manifested much interest in preventive medicine. At one time he taught in a veterinary school and was Vice-president of the Montreal Veterinary Medical Association. He became familiar with animal diseases often by actual postmortem experience. He was especially interested in those transmissible to people. Early in his career he gave a lecture on the contagious character of bovine tuberculosis and expressed the belief that tuberculosis was also spread by contagion in the human species. He even advocated a campaign to popularize this view long before most physicians considered the disease contagious. Later he said, "A last word on the subject of tuberculosis to the general practitioner. *The leadership of the battle against this scourge is in your hands. Much has been done, much remains to do. By early diagnosis and prompt, systematic treatment of individual cases, by striving in every possible way to improve the social condition of the poor, by joining actively in the work of the local and national antituberculosis societies you can help in the most important and the most hopeful campaign ever undertaken by the profession.*"

Osler's extensive practice and teaching included all known abnormal conditions of the chest including the heart. At the time of his 1892 address, there was no x-ray or bronchoscope to assist in diagnosis. The tuberculin test was just being introduced. Wassermann had not developed his test, and there was none specific for any other disease. There was no immunizing agent for a common communicable disease except smallpox. There was no known drug specific for any disease. There was no pulmonary or heart surgery.

However, with keen powers of observation, an analytical mind, and clear vision he made one contribution after another. He stimulated students and graduates in medicine. Indeed, his influence played a dominant role in promoting progress of the decades to follow.

When Doctor Paul White graduated from Harvard Medical School in 1911, the x-ray and bronchoscope, although not used extensively, were available. When he delivered his address in 1957, no communicable disease had been eradicated, but such control had been accomplished that the average length of life had increased to approximately 70 years. Geriatrics had become an important branch of medical science. Degenerative diseases had become more prevalent because so many people were living into the age period when they occur. He had seen various antimicrobial

drugs introduced and had used them. He had seen the heart yield many of its secrets to the surgeon. He had contributed significantly to knowledge of cardiovascular conditions and diseases. More than any other person he was responsible for the development of practical electrocardiography. Indeed, he had for some time been recognized as his country's foremost cardiologist.

Although 65 years elapsed between these two addresses, the authors discussed several similar topics. For example, they emphasized importance of research. Osler was particularly interested in laboratory developments while White emphasized the importance of research leading to the prevention of such conditions as rheumatic fever, hypertension and severe coronary and aortic sclerosis.

Concerning preventive measures, Doctor White said we must ". . . pick out the candidates who need the application of these measures. It would be wasteful both in time, energy and money to apply to 100 per cent of our population strict measures of preventive medicine that actually may apply to only 5, 10 or 25 per cent of the population."

Both authors warned against one of the most unfortunate practices of the medical profession even today. Doctor Osler said, "but we, the doctors, are so fallible, ever beset with the common and fatal facility by reaching conclusions from superficial observations, and constantly misled by the ease with which our minds fall into the ruts of one or two experiences."

Doctor White emphasized the "tremendous importance" of long follow-up of cases and how it was through the correction of errors in the course of follow-up studies that he and his associates were able to contribute new data concerning such conditions as pulmonary embolism, acute cor pulmonale, chronic constrictive pericarditis, coronary heart disease and the range of the normal heart. He stated that long follow-up is an opportunity and an obligation of the practicing physician. He pointed out that, unfortunately, most of the clinical research data that have been recorded are concerned with short-term studies. He cited that a long follow-up of 25 years or more of 200 cases of his own of severe coronary thrombosis seen in the decade from 1921 to 1930 inclusive was responsible for his belief in a favorable prognosis for President Eisenhower once he had recovered from the acute process.

Doctor White said, ". . . much of the temporary nature of the enthusiasm about some new medical or surgical procedure is due to the failure to establish adequate controls."

Both speeches recognized the importance of intermingling of physicians of all parts of the world. Doctor Osler mentioned several nations and emphasized the value of keeping in touch with laboratories and physicians in various parts of the world so as to be acquainted with their problems, their methods, and their new developments.

Doctor White, a world traveler, strongly recommended that at every opportunity one should meet physicians and scientific medical workers in other countries. This leads not only to greater knowledge which will help

all over the world, but also establishes international friendship and fosters eventually international peace.

These physicians kindled fires in many of their students and others through their books and published articles which will long continue to glow, lighting the way to new achievements and to the ultimate goal of the medical profession, embodying peace, happiness, longevity and efficiency for humanity everywhere.

The Patient Leads the Way*

PAUL D. WHITE, M.D., F.C.C.P.
Boston, Massachusetts

It is with great appreciation of the honor and opportunity to speak to you today that I accepted your kind invitation. These are the most exciting days in all history, that of medicine as well as that of the world. It is a choice time to be alive and to have any opportunity to take part in the evolution of science and of society from the dark ages to the dawn of what we may all hope will be that of a new civilization. I congratulate you on entering your chosen profession at this particular time in history.

It may seem trite to re-emphasize the old truth that the science and profession of medicine are based on an infinite number of individual patients with all their somatic and psychic problems. This fact is, however, what makes medicine both so difficult and at the same time so fascinating. I would like briefly today to review at least a few of these problems and to urge all of you who are about to graduate from the first stage of your medical careers to expose yourself as fully as you can to the patient himself at the very start, preferably before you begin any of your very specialized careers or at least as soon as you can. It would be helpful all the rest of your lives to spend a few years, if not in full, at least in adequate part, with sick people and with the immediate candidates for disease of which there are now being discovered an increasingly large number. It is a fact after all that the entire structure of our current complex medical edifice is based on the patient whether it be private practice or teaching or research or public health. Thus, the *patient leads the way.* He is the cornerstone or better called the keystone of the arch.

I myself regret that I took so little time at the beginning of my own medical career to do what I am advising you to do, but there always seems too much need of hurry at first; in retrospect this haste often proves to be unnecessary. I did however, have one great early advantage. My father was a family doctor. Both in my boyhood and later when I was studying medicine I had the opportunity to watch and at times even to help him in his practice.

1. *The Patient Himself. Heredity and Environment.* Now for some of the lessons learned from my own experience and from that of many of

*Graduation Address, Medical School of University of Minnesota, Minneapolis, June 14, 1957.

my teachers and colleagues. In the first place, other things being equal, the more one becomes acquainted with a patient the better usually are the results, not only in diagnosis but also in prognosis and treatment. Thus it more than pays in the end to take plenty of time both with new patients and with old. Often under pressure I have been told by a patient or indeed even by his physician, that it would take only 10 or 15 minutes to examine and treat a particular case. Such might be true if one dealt only with a very mild traumatic lesion or a cinder under the eyelid but I have always replied that for a new case of my own, consisting generally, of course, of some cardiovascular difficulty, I require a minimum of one and one fourth to one and one half hours, some of that time being spent in beginning an acquaintanceship. A "curbstone" type of examination or consultation is bad medicine. Of course, here in acquaintanceship with the patient, the family doctor has the advantage over any casual consultant unless as sometimes happily takes place in my own practice, the consultant too can become well acquainted with the patient. It is better still if that acquaintanceship can be enlarged to include the patient's family or at least the most important member or members thereof so far as the patient is concerned, that is, husband or wife, parents or children. Through such acquaintanceship one can discover important facts or clues both about the patient himself, that is, the host, and about his environment, that is, the agent or agents. I shall come back to this point again later.

I shall never forget the annoyance caused a friend of mine who lived in Austria by a medical professor whom he consulted and who didn't have time or take the time to listen to my friend's account of his symptoms and their occurrence, but hastily made an examination and wrote a prescription, confiding in no way in the patient himself. The professor missed the whole problem. This attitude happily is rapidly changing, even in the old world where it used to flourish. Now the patient is usually taken into the doctor's confidence to help him in his work. This cooperation is mutually helpful.

I would interpolate here a brief remark which has long been on the tip of my tongue when I have been exposed to clinicopathological conferences (CPC's), namely that the doctor who is trying to solve a difficult diagnostic problem is at a considerable disadvantage because he has never actually seen the patient. However, a compensation is that he almost always has the justified suspicion that the case is going to be at least a rare one or even a unique one. I always wonder when I shall be presented with a problem case who happens to have a perfectly normal heart and circulation.

So far as the patient himself is concerned one of the immediately helpful results of the acquaintanceship and time to inquire into the family history is the acquisition of some knowledge about his heredity, a much neglected aspect of our history-taking and diagnostic, prognostic, and therapeutic program of the present day. All of us who have practiced medicine for many years know that heredity counts heavily. I have been so much impressed by this that recently when I was asked to give the annual Oration of the Massachusetts Medical Society I discussed the subject under the

title "Genes, The Heart, and Destiny." This was published in a recent number of the *New England Journal of Medicine*. You may care to consult it.

In summary of that article at the present time I emphasized three points:—

First, the need of the physician himself to inquire more fully into the antecedents of the patients, that is, the duration of life and the diseases not only of the parents and siblings but of all four grandparents and perhaps other relatives. This takes time but it is time well spent.

Second, inasmuch as the patient himself often has only a vague knowledge about his grandparents I have recommended that every family now resume the keeping of a record of family data, births, marriages, and deaths in the old family Bible or some substitute thereof. This record should make mention of diseases and vital autopsy information for the sake of the descendants of that family. We and they must think of the future.

Third, I begged for the training and utilization of more expert human geneticists. We have far too few in this country today.

Also, of importance as I have just suggested in addition to obtaining a good history of family, past illnesses, and habits of the patient is information about some of the details of his environment. Nearly every family has problems which include illnesses and accidents, dissensions, financial reverses, and the like. Uncovering some of these problems, privately recorded, of course, can sometimes reveal a very important clue.

2. *The Psyche and the Soma.* The second problem rightly coming into great prominence now is that of the relationship of the psyche and the soma, both in normal and in pathological physiology. Of course, psychosomatic medicine itself is as old as the hills. In fact, it was the only medicine available in antiquity and practically even up to my father's day, as evidenced by his very effective use of sugar pills with little else available at the time when he began to practice in the 1880's, except for a few of the more powerful drugs and the beginning of aseptic surgery. Gradually, as definitive and curative medicine has become possible for many infectious diseases and traumatic lesions, somatic therapy has advanced by leaps and bounds until with the last generation it has almost completely superseded psychosomatic therapy which in its turn now is in the process of being revived as something new. We can not, however, separate the influences on total health of the actions of the psyche and of the soma. They react on each other in a most impressive way.

While we are increasing the scope of our dramatic curative medicine and surgery (witness two examples in the use of antibiotics and in cardiovascular surgical technics) with the wonderful effects thereof on longevity and on the health of the psyche, we must remember that much of the benefit of medical attention, past, present, and future, comes through the strengthening or the actual inculcation of certain positive virtues which we know can act on the body helpfully. Exactly how they act remains mostly to be discovered. These positive virtues include courage, patience,

and optimism. Certainly one of the rules of the practicing physician is to remember to use these ancient resources as well as the modern technics of the present golden age of medicine and surgery. This is the challenge that faces the young physician today who may be overimpressed by his chemical and physical therapeutic armamentarium.

3. *Diagnosis.* And now we come to some advice about diagnosis that may be helpful to you from a long experience in medical practice. First and most important of all in revealing clues is a meticulous history of the patient, of his past illnesses, of his habits, of his environment, of his family, and of his current illness. It is best as a rule to let him begin with the tale of his present difficulties and then to follow by asking specifically for other information, as just noted, any scrap of which may give us the answer in a difficult case. I have repeatedly urged in the past that it is better for the doctor himself to take the patient's history than to delegate it to another (colleague, assistant, nurse or secretary) whether or not experienced in this delicate technic. The questioner should be the patient's doctor himself. This is, of course, one way of becoming acquainted with the patient and his family and of learning the background. The time spent in taking this history is incidentally invaluable from the standpoint of simple observation of the patient. Such observation in itself frequently yields clues that cannot be adequately recorded on the record and which cannot be obtained by reading a history taken by someone else or presented by a pathologist at a CPC exercise.

Second, so far as diagnosis is concerned, one can with experience collect the necessary objective data and yet not include an exhaustive series of tests. It is naturally essential to have early in the process of visits of the patient to office or hospital such fundamental data as the urine and blood examination and from the standpoint of the chest, an x-ray film or fluoroscopic examination and an electrocardiogram. Other technics can be resorted to as needed. I have been much encouraged of late years in being presented with uniform records of electrocardiogram, x-ray film, tests of the blood, and other tests if needed, when I have been consulted about patients in a number of different parts of the world.

Finally, I would add that two of the most important aids to me in improving my own diagnostic ability have been: First, the utilization of errors that I have made or that are being made by others, either of omission or commission, and second, a persistent effort to obtain autopsies at death of patients whom I have followed for years. These two procedures have been invaluable. One undoubtedly can learn new things even in the field of medicine itself by checking errors of diagnosis, especially if they have been repeated and, of course, also by careful postmortem analyses. Don't discard or file away indefinitely your difficult, obscure, or troublesome cases, especially if they have been the occasion of errors in diagnosis, prognosis, or therapy. It is possible in important cases to obtain autopsies by informing colleagues who may know the patient and informing the family too, of the importance of the long follow-up to the time of death. On several occasions years ago, we persevered in getting permission for autopsies

even after funeral and burial with results that were helpful to many thousands of sick people. It was through the correction of errors in the course of follow-up studies that my associates and I were able to contribute new data concerning pulmonary embolism and the acute cor pulmonale, chronic constrictive pericarditis, the WPW electrocardiographic syndrome, coronary heart disease, and the range of the normal heart.

4. *Prognosis.* One of the weakest aspects of our medical practice today is that of prognosis, in large part because of its difficulties and of our failure to spend enough time on its background. I would like to quote briefly from the Billings Lecture which I gave before the Section of Medicine of the American Medical Association a few years ago. Before I do, however, I want to emphasize the tremendous importance of *the long follow-up,* an opportunity and an obligation of the practicing physician. One of the defects of medical teaching in recent decades has been the lack of adequate follow-up by some of the heads of medicine themselves, many of whom, of course, have lived a somewhat peripatetic life or have not had time to devote to this particular aspect of medicine. Part time teachers of medicine who are in active practice and general practitioners, therefore, have an important obligation which they have not adequately utilized. Most of the clinical research data that have been recorded are concerned with short time studies. May I add that a long follow-up of twenty-five years or more of 200 cases of my own of severe coronary thrombosis seen in the decade from 1921 to 1930 inclusive was responsible for our belief in a favorable prognosis for President Eisenhower once he had recovered from the acute process. He belonged to the third of the survivors of the acute process who were free from symptoms after recovery and who had little or no cardiac enlargement.

Now the quotations from the Billings Lecture.

"Although the importance of prognosis (preknowledge or forecasting) in medicine was clearly appreciated by Hippocrates, it has progressed very little and very slowly through the many centuries in contrast to the scientific development of etiology, pathology, diagnosis, and treatment. In the Dark and Middle Ages it drifted almost wholly into superstition. It still remains a stepchild in medical advance partly because it is a difficult subject and partly because, for some reason or other, it has inadequately been studied scientifically. The few sentences devoted to it in the account of almost any disease or condition in almost all textbooks and papers are little more than a sop to the conscience. In cases of cardiovascular disease, the statement of prognosis often ends with the word 'guarded,' largely to play safe. Granted that we cannot foretell the future with any certainty, I feel sure, nevertheless, that we can do better than we have in the past, or are doing now, by approaching the subject more scientifically and seriously. We have more facts and knowledge on which to base our prognoses than we utilize; we should call more than we do on the laws of chance in both our written opinions of prognosis of any disease and our discussion of the prognosis of any individual case with the patient himself, with his family, or with fellow physicians.

"Here and there, however, in the past there have been physicians who have pointed to the importance of developing a more scientific attitude toward prognosis. For example, James Mackenzie, in the third edition of his book entitled 'Diseases of the Heart,' published in 1913, wrote as follows in chapter 45 entitled 'Prognosis.' 'I am rather afraid that our profession as a body does not recognize sufficiently its responsibility in regard to prognosis. When an individual submits himself for an opinion he does so with such implicit confidence that the verdict given may alter the whole tenor of his life . . . A serious responsibility is thrown upon every practitioner at times in advising upon certain questions. 'Should a man give up his business? This is a question on which advice is constantly sought and whether the individual be a statesman or a laborer, the greatest care is necessary in formulating an answer. If a practitioner seeks for guidance in the textbooks he finds merely general views which he cannot apply to the individual case.'

"The greatest difficulty in prognosis lies in its complication. There are more factors to be taken into consideration, especially in cardiovascular prognosis, than there are in either diagnosis or treatment. These factors are never just the same in any two cases, and so the prognoses listed in books or papers under the various kinds of heart disease are necessarily very rough estimates; the averages actually apply to very few cases. The difficulties in determining the outcome are illustrated in the discussions of prognosis in the sections on vascular hypertension, congenital heart disease, subacute bacterial endocarditis, and other common forms of heart disease in Cecil and Loeb's 'Textbook of Medicine.' In the fourth edition of my book 'Heart Disease,' published in 1951, I combined 'prognosis' with 'course' because of the difficulty of writing adequately about prognosis as an isolated subject.

"There are many factors that combine to form the basis for cardiovascular prognosis in any given case. Thereon rest the foundations of the principles and practice of prognosis that should rightly become, with time, a science rather than an art. I will present 10 factors, although another might well be added representing chance and unexpected circumstances beyond our control or even beyond our knowledge. Often, of course, the experienced physician does, in the course of his career, acquire some considerable skill in prognosis, but this is often hit or miss and without conscious analysis of the separate factors that I will present."

These ten factors which I cited are as follows:—

1) Heredity.
2) Age, in which often the prognosis deteriorates with age but by no means always (many people outgrow their troubles, such as angina pectoris).
3) Sex, young and middle aged men being hit much harder than women both by hypertension and by serious coronary heart disease.
4) The type of heart disease.
5) The degree of the disease.

6) The stage of the disease.
7) The adequacy of treatment.
8) Medical knowledge of the time.
9) Patient cooperation.
10) The attitude of all concerned, including physician, patient, family, friends, and even on occasion the community too.

Twenty-five years ago I wrote an article entitled "Optimism in the Treatment of Cardiovascular Disease," based on a group of patients who had gotten along better than had been expected. This could well be repeated today.

5. *Treatment.* Less needs to be said to you about the evolution of treatment than about the other problems of medicine and surgery because of the very active developments in therapy both in research and in practice. It is here in particular, as well as in diagnosis, that the greatest advances have come in the last generation. Nevertheless, even here it is well to bear in mind certain important principles. In the first place, much of the temporary nature of the enthusiasm about some new medicine or surgical procedure is due to the failure to establish adequate controls. It is of vital importance to remember the motto that Walter Cannon and others so often drummed into our ears: "Cherchez le controle." Sometimes these measures die out altogether, but often they subside to a state of some usefulness though far less than originally heralded. It may be best to follow the old adage which goes as follows:

"Be not the first by whom the new is tried
Nor yet the last to throw the old aside."

Attention to a happy mean between the two extremes is certainly desirable in the active practice of medicine.

A second very important principle to remember in practice is that of avoiding polypharmacy. The shotgun prescription used to be a favorable therapeutic tool, but it is now long outmoded except in a few parts of the world where I have still found it in operation. There is a fascination of the public to submit itself to multiple piqures or hypodermic, intramuscular, or intravenous injections, and to the laying on of hands or of absent treatment. The most experienced and able doctors of the present day, however, realize that it is better to treat as simply as possible, at the same time presenting as optimistic an attitude as is justified for the sake of the patient's morale.

Finally, in the face of great discouragement and of incurable disease, one can maintain some degree of hope both in one's own mind and in that of the patient since justifiably both he and the patient may pray that something new in the amelioration or cure of the disease may be just around the corner.

6. *Research.* In every field of medicine today, including all areas of the soma and of the psyche, research is not only beginning to be carried out but also is being applied. Much of it is basic and every worker in a special field should welcome basic research that deals with all fields of

biology whether in biophysics, in biochemistry, or in psychology. In fact, some of the most interesting recent research has revealed a chemical basis for some of the abnormal psychology that has puzzled man since the dawn of civilization. We may hope that this application of basic research can be developed with the support, both morally and materially, of public and of private agencies hand in hand. This will lead eventually to the application of my next subject, namely

7. *Preventive Medicine.* Only yesterday I engaged in a fascinating conference with a physician because of bereavement in his own family. He was, as I, much impressed with the importance of preventive measures. Many members of the medical profession have been very casual in any effort first to discover candidates for certain diseases (as applied to cardiovascular disease, this would include rheumatic fever, hypertension, and severe coronary and aortic sclerosis), and second, to apply common sense measures of a preventive nature to such candidates. As I said at the beginning of this address, we must consider not only environmental factors, that is, the agent or agents directly responsible for disease, but the host, that is, the candidate most likely to react adversely to such environmental factors. Actually very little application of this has been done in medical practice. It is obviously more important to protect candidates from disease than it is to treat them after they have gotten the disease.

Although there is much still to be learned by epidemiological research, we do have some knowledge of the importance of simple measures of hygiene, such as the harmfulness of obesity as proved by Life Insurance statistics, the harmful effects of excessive tobacco in the presence of high blood pressure or hyperreactivity, and of irritability of stomach, lungs, and circulation, including the heart. We also know of the lack of protection that comes from alcohol which has been given too much credit as a useful agent. I have seen too many young people hurt both by tobacco and alcohol to remain passively acquiescent in heavy habituation to these agents, at least in certain cases. A patient whom I saw only yesterday is another illustration of what can actually be done by protective measures. This man began to have angina pectoris 22 years ago in his early 30's. He was found later to have a high serum cholesterol content. When I first saw him 12 years ago, certain measures were strongly urged on him, to reduce his overweight, to eat sparingly of fat, to omit tobacco, and to take regular exercise. To these measures of positive health he has adhered and today he is well, having outgrown his angina pectoris, doubtless through the development of a collateral circulation without the accumulation of enough additional atherosclerosis in his coronary artery walls to cause new trouble. He has kept his weight strictly down, has eaten sparingly of fat, and has taken regular exercise; for example, he walks three miles daily before breakfast. I have a strong belief that he has not just been lucky, but that he deserves his "good luck."

Thus in public health in the future we must not only determine what can be done, as Herman Biggs asked more than 50 years ago, to protect our citizens and the youth of tomorrow from the so-called chronic diseases

of today, but we must also pick out the candidates who need the application of these measures. It would be wasteful both in time, energy, and money to apply to a 100 per cent of our population, strict measures of preventive medicine that actually may apply to only 5, 10, or 25 per cent of the population. Nevertheless, in general, in our current state of ignorance we can rightfully advise for the people at large common sense measures of life which would include the avoidance of too much slavery to the push-button automobile and television existence of today. I would agree from my experience of the last few years that, for most of us at least, a sensible limitation of fat intake, to say 25 to 30 per cent of the total calories, as advised by Ancel Keys, the establishment and maintenance of an optimal weight, and a habit of regular exercise are highly desirable, at least unless and until we learn otherwise.

8. *International Medicine.* Finally, I want to recommend to you that when you have the opportunity in the future to meet physicians and scientific medical workers of other countries either here at home or in their own homeland you avail yourselves of such opportunities. One learns a good deal from the physicians of other countries. We can be mutually helpful. Furthermore, we ourselves can learn for the benefit of our own health from researches in which we may join in other countries. Cooperative international cardiovascular or other medical research should ultimately result not only in greater knowledge which will help all of us all over the globe, but should also establish international friendships and foster eventually international peace. We doctors have perhaps only a small role to play in such an opportunity, but small as it is, let us play it. I often feel that if we physicians could take over international relationships, peace could descend upon the world. This may be a far cry from reality but nevertheless physicians do take care of leaders in business, in the professions, and in government throughout the world. Thus they do have willy-nilly an important responsibility which is not that of playing politics but that of helping to establish friendly relations in a completely impartial way.

In conclusion, I am sure that I have omitted much that might have been added in the way of helpful advice to you and quite possibly have said some things that may not turn out to be of great importance. Nevertheless the experience of a doctor who has lived through the last few decades can be, I believe, of some value to you and especially a stimulus if he has, as has been my good fortune, enjoyed every moment of this fascinating profession of ours in which we are working together today.

Teacher and Student*

SIR WILLIAM OSLER

Truly it may be said today that in the methods of teaching medicine the old order changeth, giving place to new, and to this revolution let me briefly refer, since it has an immediate bearing on the main point I wish to make in the first portion of my address. The medical schools of the country have been either independent, University, or State Institutions. The first class, by far the most numerous, have in title University affiliations, but are actually devoid of organic union with the seats of learning. Necessary as these bodies have been in the past, it is a cause for sincere congratulation that the number is steadily diminishing. Admirable in certain respects— adorned too in many instances by the names of men who bore the burden and heat of the day of small things, and have passed to their rest amid our honoured dead—the truth must be acknowledged that the lamentable state of medical education in this country twenty years ago was the direct result of the inherent viciousness of a system they fostered. Something in the scheme gradually deadened in the professors all sense of the responsibility until they professed to teach (mark the word), in less than two years, one of the most difficult arts in the world to acquire. Fellow teachers in medicine, believe me that when fifty or sixty years hence some historian traces the development of the profession in this country, he will dwell on the notable achievements, on the great discoveries, and on the unwearied devotion of its members, but he will pass judgment—yes, severe judgment—on the absence of the sense of responsibility which permitted a criminal laxity in medical education unknown before in our annals. But an awakening has come, and there is sounding the knell of doom for the medical college, responsible neither to the public nor the profession.

The schools with close university connections have been the most progressive and thorough in this country. The revolution referred to began some twenty years ago with the appearance of the President of a well-known University at a meeting of its medical faculty with a peremptory command to set their house in order. Universities which teach only the Liberal Arts remain today, as in the middle ages, Scolae minores, lacking the technical faculties which make the Scolae majores. The advantages of this most natural union are manifold and reciprocal. The professors in a University medical school have not the independence of which I have spoken, but are under an influence which tends constantly to keep them at a high level: they are urged by emulation with other faculties to im-

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**See Holmes on President Eliot in *Life and Letters of O. W. Holmes*, 1896, ii, 187, 188, 190.

prove the standard of work, and so are given a strong stimulus to further development.

To anyone who has watched the growth of the new ideas in education it is evident that the most solid advances in methods of teaching, the improved equipment, clinical and laboratory, and the kindlier spirit of generous rivalry—which has replaced the former debased method of counting heads as a test of merit—all these advantages have come from a tightening of the bonds between the medical school and the University.

And lastly there are the State schools, of which this college is one of the few examples. It has been a characteristic of American Institutions to foster private industries and to permit private corporations to meet any demands on the part of the public. This idea carried to extreme allowed the unrestricted manufacture—note the term—of doctors, quite regardless of the qualifications usually thought necessary in civilized communities—of physicians who may never have been inside a hospital ward, and who had, after graduation, to learn medicine somewhat in the fashion of the Chinese doctors who recognized the course of the arteries of the body, by noting just where the blood spurted when the acupuncture needle was inserted. So far as I know, State authorities have never interfered with any legally instituted medical school, however poorly equipped for its work, however lax the qualifications for license. Not only has this policy of non-intervention been carried to excess, but in many States a few physicians in any town could get a charter for a school without giving guarantees that laboratory or clinical facilities would be available. This anomalous condition is rapidly changing, owing partly to a revival of loyalty to higher ideals within the medical profession, and partly to a growing appreciation in the public of the value of physicians thoroughly educated in modern methods. A practical acknowledgement of this is found in the recognition in three States at least of medicine as one of the technical branches to be taught in the University supported by the people at large.

But it is a secondary matter, after all, whether a school is under State or University control, whether the endowments are great or small, the equipments palatial or humble; the fate of an institution rests not on these; the inherent, vital element, which transcends all material interests, which may give to a school glory and renown in their absence, and lacking which, all the "pride, pomp and circumstance" are vain—this vitalizing element, I say, lies in the men who work in its halls, and in the ideals which they cherish and teach. There is a passage in one of John Henry Newman's Historical Sketches which expresses this feeling in terse and beautiful language: "I say then, that the personal influence of the teacher is able in some sort to dispense with an academical system, but that system cannot in any way dispense with personal influence. With influence there is life, without it there is none; if influence is deprived of its due position, it will not by those means be got rid of, it will only break out irregularly, dangerously. An academical system without the personal influence of teachers upon pupils, is an Arctic winter; it will create an ice-bound, petrified, cast-iron University, and nothing else."

Naturally from this standpoint the selection of teachers is the function of highest importance in the Regents of a University. Owing to local conditions the choice of men for certain of the chairs is restricted to residents in the University town, as the salaries in most schools of this country have to be supplemented by outside work. But in all departments this principle should be acknowledged and acted upon by trustees and faculties, and supported by public opinion—that the very best men available should receive appointments. It is gratifying to note the broad liberality displayed by American colleges in welcoming from all parts teachers who may have shown any special fitness, emulating in this respect the liberality of the Athenians, in whose porticoes and lecture halls the stranger was greeted as a citizen and judged by his mental gifts alone. Not the least by any means of the object lessons taught by a great University is that literature and science know no country, and, as has been well said, acknowledge "no sovereignty but that of the mind, and no nobility but that of genius." But it is difficult in this matter to guide public opinion, and the Regents have often to combat a provincialism which is as fatal to the highest development of a University as is the shibboleth of a sectarian institution.

To paraphrase the words of Matthew Arnold, the function of the teacher is to teach and to propagate the best that is known and taught in the world. To teach the current knowledge of the subject he professes—sifting, analyzing, assorting, laying down principles. To propagate, i.e., to multiply, facts on which to base principles—experimenting, searching, testing. The best that is known and taught in the world—nothing less can satisfy a teacher worthy of the name, and upon us of the medical faculties lies a bounden duty in this respect, since our Art, co-ordinate with human suffering, is cosmopolitan.

There are two aspects in which we may view the teacher—as a worker and instructor in science, and as practitioner and professor of the art; and these correspond to the natural division of the faculty into the medical school proper and the hospital.

In this eminently practical country the teacher of science has not yet received full recognition, owing in part to the great expense connected with his work, and in part to carelessness or ignorance in the public as to the real strength of a nation. To equip and maintain separate laboratories in Anatomy, Physiology, Chemistry (physiological and pharmacological), Pathology and Hygiene, and to employ skilled teachers, who shall spend all their time in study and instruction, require a capital not today at the command of any medical school in the land. There are fortunate ones with two or three departments well organized, not one with all. In contrast, Bavaria, a kingdom of the German Empire, with an area less than this State, and a population of five and a half millions, supports in its three University towns flourishing medical schools with extensive laboratories, many of which are presided over by men of world wide reputation, the steps of whose doors are worn in many cases by students who have crossed the Atlantic; seeking the wisdom of methods and the virtue of inspiration not easily accessible at home. But there were professors in Bavarian

medical schools before Marquette and Joliet had launched their canoes on the great stream which the intrepid La Salle had discovered, before Du Lhut met Father Hennepin below the falls of St. Anthony; and justice compels us to acknowledge that while winning an empire from the backwoods the people of this land had more urgent needs than laboratories of research. All has now changed. In this State, for example, the phenomenal growth of which has repeated the growth of the nation, the wilderness has been made to blossom as the rose, and the evidences of wealth and prosperity on every side almost constrain one to break out into the now old song, "Happy is that people that is in such a case."

But in the enormous development of material interests there is danger lest we miss altogether the secret of a nation's life, the true test of which is to be found in its intellectual and moral standards. There is no more potent antidote to the corroding influence of Mammon than the presence in a community of a body of men devoted to science, living for investigation and caring nothing for the lust of the eyes and the pride of life. We forget that the measure of the value of a nation to the world is neither the bushel nor the barrel, but *mind;* and that wheat and pork, though useful and necessary, are but dross in comparison with those intellectual products which alone are imperishable. The kindly fruits of the earth are easily grown; the finer fruits of the mind are of slower development and require prolonged culture.

Each one of the scientific branches to which I have referred has been so specialized that even to teach it takes more time than can be given by a single professor, while the laboratory classes also demand skilled assistance. The aim of a school should be to have these departments in the charge of men who have, first, *enthusiasm,* that deep love of a subject, that desire to teach and extend it without which all instruction becomes cold and lifeless; secondly, *a full personal knowledge of the branch taught;* not a second-hand information derived from books, but the living experience derived from experimental and practical work in the best laboratories. This type of instructor is fortunately not rare in American schools. The well-grounded students who have pursued their studies in England and on the Continent have added depth and breadth to our professional scholarship, and their critical faculties have been sharpened to discern what is best in the world of medicine. It is particularly in these branches that we need teachers of wide learning, whose standards of work are the highest known, and whose methods are those of the masters in Israel. Third, men are required who have *a sense of obligation,* that feeling which impels a teacher to be also a contributor, and to add to the stores from which he so freely draws. And precisely here is the necessity to know the best that is taught in this branch, the world over. The investigator, to be successful, must start abreast of the knowledge of the day, and he differs from the teacher, who, living in the present, expounds only what is current, in that his thoughts must be in the future, and his ways and work in advance of the day in which he lives. Thus, unless a bacteriologist has studied methods thoroughly, and is familiar with the extraordinarily complex flora asso-

ciated with healthy and diseased conditions, and keeps in touch with every laboratory of research at home and abroad, he will in attempting original work, find himself exploring ground already well-known, and will probably burden an already over-laden literature with faulty and crude observations. To avoid mistakes, he must know what is going on in the laboratories of England, France and Germany, as well as in those of his own country, and he must receive and read six or ten journals devoted to the subject. The same need for wide and accurate study holds good in all branches.

Thoroughly equipped laboratories, in charge of men thoroughly equipped as teachers and investigators, is the most pressing want today in the medical schools of the country.

The teacher as a professor and practitioner of his art is more favored than his brother, of whom I have been speaking; he is more common, too, and less interesting; though in the eyes of "the fool multitude who choose by show" more important. And from the standpoint of medicine as an art for the prevention and cure of disease, the man who translates the hieroglyphics of science into the plain language of healing is certainly the more useful. He is more favoured inasmuch as the laboratory in which he works, the hospital, is a necessity in every center of population. The same obligation rests on him to know and to teach the best that is known and taught in the world—on the surgeon the obligation to know thoroughly the scientific principles on which his art is based, to be a master in the technique of his handicraft, ever studying, modifying, improving; on the physician, the obligation to study the natural history of diseases and the means for their prevention, to know the true value of regimen, diet and drugs in their treatment, ever testing, devising, thinking; and upon both, to teach to their students habits of reliance, and to be to them examples of gentleness, forbearance and courtesy in dealing with their suffering brethren.

I would fain dwell upon many other points in the relation of the hospital to the medical school—on the necessity of ample, full and prolonged clinical instruction, and on the importance of bringing the student and the patient into close contact, not through the cloudy knowledge of the amphitheatre, but by means of the accurate, critical knowledge of the wards; on the propriety of encouraging the younger men as instructors and helpers in ward work; and on the duty of hospital physicians and surgeons to contribute to the advance of their art—but I pass on with an allusion to a very delicate matter in college faculties.

From one who, like themselves, has passed *la crise de quarante ans*, the seniors present will pardon a few plain remarks upon the disadvantages to a school of having too many men of mature, not to say riper, years. Insensibly, in the fifth and sixth decades, there begins to creep over most of us a change, noted physically among other ways in the silvering of the hair and that lessening of elasticity, which impels a man to open rather than to vault a five-barred gate. It comes to all sooner or later; to some it is only too painfully evident, to others it comes unconsciously, with no pace perceived. And with most of us this physical change has its mental

equivalent, not necessarily accompanied by loss of the powers of application or of judgment; on the contrary, often the mind grows clearer and the memory more retentive, but the change is seen in a weakened receptivity and in an inability to adapt oneself to an altered intellectual environment. It is this loss of mental elasticity which makes men over forty so slow to receive new truths. Harvey complained in his day that few men above this critical age seemed able to accept the doctrine of the circulation of the blood, and in our own time it is interesting to note how the theory of the bacterial origin of certain diseases has had, as other truths, to grow to acceptance with the generation in which it was announced. The only safeguard in the teacher against this lamentable condition is to live in, and with the third decade, in company with the younger, more receptive and progressive minds.

There is no sadder picture than the Professor who has outgrown his usefulness, and, the only one unconscious of the fact, insists with a praiseworthy zeal, upon the performance of duties for which the circumstances of the time have rendered him unfit. When a man nor wax nor honey can bring home, he should, in the interests of an institution, be dissolved from the hive to give more labourers room; though it is not every teacher who will echo the sentiment—

> Let me not live . . .
> After my flame lacks oil, to be the snuff
> Of younger spirits whose apprehensive senses
> All but new things disdain.

As we travel farther from the east, our salvation lies in keeping our faces toward the rising sun, and in letting the fates drag us, like Cacus his oxen, backward into the cave of oblivion.

III

Students of Medicine, Apprentices of the Guild, with whom are the promises, and in whom center our hopes—let me congratulate you on the choice of calling which offers a combination of intellectual and moral interests found in no other profession, and not met with at all in the common pursuits of life—a combination which, in the words of Sir James Paget, "offers the most complete and constant union of those three qualities which have the greatest charm for pure and active minds—novelty, utility, and charity." But I am not here to laud our profession; your presence here on these benches is a guarantee that such praise is superfluous. Rather allow me, in the time remaining at my disposal, to talk of the influences which may make you good students—now in the days of your pupilage, and hereafter when you enter upon the more serious duties of life.

In the first place, acquire early the *Art of Detachment*, by which I mean the faculty of isolating yourselves from the pursuits and pleasures incident to youth. By nature man is the incarnation of idleness, which quality alone, amid the ruined remnants of Edenic characters, remains in all its primitive intensity. Occasionally we do find an individual who takes to toil as others take to pleasure, but the majority of us have to wrestle hard

with the original Adam, and find it is no easy matter to scorn delights and live laborious days. Of special importance is this gift to those of you who reside for the first time in a large city, the many attractions of which offer a serious obstacle to its acquisition. The discipline necessary to secure this art brings in its train habits of self-control and forms a valuable introduction to the sterner realities of life.

I need scarcely warn you against too close attention to your studies. I have yet to meet a medical student, the hey-day in whose blood had been quite tamed in his college days; but if you think I have placed too much stress upon isolation in putting the Art of Detachment first in order amongst the *desiderate* let me temper the hard saying by telling you how with "labors assiduous due pleasures to mix." Ask of any active business man or leader in a profession the secret which enables him to accomplish much work, and he will reply in one word, *system;* or as I shall term it, the *Virtue of Method,* the harness without which only the horses of genius travel. There are two aspects of this subject; the first relates to the orderly arrangement of your work, which is to some extent enforced by the roster of demonstrations and lectures, but this you would do well to supplement in private study by a schedule in which each hour finds its allotted duty. Thus faithfully followed, day by day system may become at last engrained in the most shiftless nature, and at the end of a semester a youth of moderate ability may find himself far in advance of the student who works spasmodically, and trusts to *cramming.* Priceless as this virtue is now in the time of your probation, it becomes in the practicing physician an incalculable blessing. The incessant and irregular demands upon the busy doctor make it very difficult to retain, but the public in this matter can be educated, and the men who practice with system, allotting a definite time of day to certain work, accomplish much more and have at any rate a little leisure; while those who are unmethodical never catch up with the day's duties and worry themselves, their *confreres,* and their patients.

The other aspect of method has a deeper significance, hard for you to reach, not consoling when attained, since it lays bare our weaknesses. The practice of medicine is an art, based on science. Working with science, in science, for science, it has not reached, perhaps never will, the dignity of a complete science, with exact laws, like astronomy or engineering. Is there then no science of medicine? Yes, but in parts only, such as anatomy and physiology, and the extrordinary development of these branches during the present century has been due to the cultivation of method, by which we have reached some degree of exactness, some certainty of truth. Thus we can weigh the secretions in the balance and measure the work of the heart in foot-pounds. The deep secrets of generation have been revealed and the sesame of evolution has given us fairy tales of science more enchanting than the Arabian Nights' entertainment. With this great increase in our knowledge of the laws governing the processes of life, has been a corresponding, not less remarkable, advance in all that relates to life in disorder, that is, disease. The mysteries of heredity are less mysterious, the operating room has been twice over robbed of its terrors; the laws of epidemics are known,

and the miracle of the threshing floor of Araunah the Jebusite, may be repeated in any town out of Bumbledom. All this change has come about by the observation of facts, by their classification, and by the founding upon them of general laws. Emulating the persistence and care of Darwin, we must collect facts with open-minded watchfulness, unbiased by crotchets or notions; fact on fact, instance on instance, experiment on experiment, facts which fitly joined together by some master who grasps the idea of their relationship may establish a general principle. But in the practice of medicine, where our strength should be lies our great weakness. Our study is man, as the subject of accidents or diseases. Were he always, inside and outside, cast in the same mould, instead of differing from his fellow man as much in constitution and in his reactions to stimulus as in feature, we should ere this have reached some settled principles in our art. And not only are the reactions themselves variable, but we, the doctors, are so fallible, ever beset with the common and fatal facility of reaching conclusions from superficial observations, and constantly misled by the ease with which our minds fall into the ruts of one or two experiences.

And third add to the Virtue of Method, the *Quality of Thoroughness*, an element of such importance that I had thought of making it the only subject of my remarks. Unfortunately, in the present arrangement of the curriculum, few of you as students can hope to obtain more than a measure of it, but all can learn its value now, and ultimately with patience become living examples of its benefit. Let me tell you briefly what it means. A knowledge of the fundamental sciences upon which our art is based—chemistry, anatomy, and physiology—not a smathering, but a full and deep acquaintance, not with all the facts, that is impossible, but with the great principles based upon them. You should, as students, become familiar with the methods by which advances in knowledge are made, and in the laboratory see clearly the paths the great masters have trodden, though you yourselves cannot walk therein. With a good preliminary training and a due apportioning of time you can reach in these three essential studies a degree of accuracy which is the true preparation for your life duties. It means such a knowledge of diseases and of the emergencies of life and of the means for their alleviation, that you are safe and trustworthy guides for your fellowmen. You cannot of course in the brief years of pupilage so grasp the details of the various branches that you can surely recognize and successfully treat all cases. But here if have mastered certain principles is at any rate one benefit of thoroughness—you will avoid the sloughs of charlatanism. Napoleon, according to Sainte Beuve, one day said when somebody was spoken of in his presence as a charlatan, "Charlatan as much as you please, but where is there not charlatanism?" Now, thoroughness is the sole preventive of this widespread malady, which in medicine is not met with only outside of the profession. Matthew Arnold, who quotes the above from Sainte Beuve, defines charlatanism as the "confusing or obliterating the distinctions between excellent and inferior, sound and unsound, or only half sound, true and untrue or half true." The higher the standard of education in a profession the less marked will be the charla-

tanism, whereas no greater incentive to its development can be found than in sending out from our colleges men who have not had mental training sufficient to enable them to judge between the excellent and the inferior, the sound and the unsound, the true and the half true. And if we of the household are not free from the seductions of this vice, what of the people among whom we work? From the days of the sage of Endor, even the rulers have loved to dabble in it, while the public of all ages have ever revelled in its methods—today, as in the time of the Father of Medicine, one of whose contemporaries (Plato) thus sketches the world old trait: "And what a delightful life they lead! they are always doctoring and increasing and complicating their disorders and always fancying they will be cured by any nostrum which anybody advises them to try."

The Art of Detachment, the Virtue of Method, and the Quality of Thoroughness may make you students, in the true sense of the word, successful practitioners, or even great investigators; but your characters may still lack that which can alone give permanence to powers—the *Grace of Humility*. As the divine Italian at the very entrance to Purgatory was led by his gentle Master to the banks of the island and girt with a rush, indicating thereby that he had cast off all pride and self-conceit, and was prepared for his perilous ascent to the realms above, so should you, now at the outset of your journey take the reed of humility in your hands, in token that you appreciate the length of the way, the difficulties to be overcome, and the fallibility of the faculties upon which you depend.

In these days of aggressive self-assertion, when the stress of competition is so keen and the desire to make the most of oneself so universal, it may seem a little old-fashioned to preach the necessity of this virtue, but I insist for its own sake, and for the sake of what it brings, that a due humility should take the place of honour on the list. For its own sake, since with it comes not only a reverence for truth, but also a proper estimation of the difficulties encountered in our search for it. More perhaps than any other professional man, the doctor has a curious—shall I say morbid?—sensitiveness to (what he regards) personal error. In a way this is right; but it is too often accompanied by a *cocksureness* of opinion which, if encouraged, leads him to so lively a conceit that the mere suggestion of mistake under any circumstances is regarded as a reflection on his honour, a reflection equally resented whether of lay or of professional origin. Start out with the conviction that absolute truth is hard to reach in matters relating to our fellow creatures, healthy or diseased, that slips in observation are inevitable even with the best trained faculties, that errors in judgment must occur in the practice of an art which consists largely of balancing probabilities; start, I say, with this attitude in mind, and mistakes will be acknowledged and regretted; but instead of a slow process of self-deception, with ever increasing inability to recognize truth, you will draw from your terrors the very lessons which may enable you to avoid their repetition.

And, for the sake of what it brings, this grace of humility is a precious gift. When to the sessions of sweet silent thought you summon up the re-

membrance of your own imperfections, the faults of your brothers will seem less grievous, and, in the quaint language of Sir Thomas Browne, you will "allow one eye for what is laudable in them." The wrangling and unseemly disputes which have too often disgraced our profession arise, in a great majority of cases, on the one hand, from this morbid sensitiveness to the confession of error, and, on the other, from a lack of brotherly consideration, and a convenient forgetfulness of our own failings. Take to heart the words of the son of Sirach, winged words to the sensitive souls of the sons of Esculapius: "Admonish a friend, it may be he has not done it; and if he have done it, that he do it no more. Admonish thy friend, it may be he hath not said it; and if he have, that he speak it not again. Admonish a friend, for many times it is a slander, and believe not every tale." Yes, many times it is a slander, and believe not every tale.

The truth that lowliness is young ambition's ladder is hard to grasp, and when accepted harder to maintain. It is so difficult to be still amidst bustle, to be quiet amidst noise; yes, "*es bildet ein Talent sich in der Stille*" alone, in the calm life necessary for continuous work for a high purpose. The spirit abroad at present in this country is not favorable to this Teutonic view, which galls the quick apprehension and dampens the enthusiasm of the young American. All the same, it is true, and irksome at first though the discipline may be, there will come a time when the very fetters in which you chafed shall be a strong defense, and your chains a robe of glory.

Sitting in Lincoln Cathedral and gazing at one of the loveliest of human works—for such the angel Choir has been said to be—there arose within me, obliterating for the moment the thousand heraldries and twilight saints and dim emblazonings, a strong sense of reverence for the minds which had conceived and the hands which had executed such things of beauty. What manner of men were they who could, in those (to us) dark days, build such transcendent monuments? What was the secret of their art? By what spirit were they moved? Absorbed in thought, I did not hear the beginning of the music, and then, as a response to my reverie and arousing me from it, rang out the clear voice of the boy leading the antiphon, "That Thy power, Thy glory and the mightiness of Thy kingdom might be known unto men." Here was the answer. Moving in a world not realized, these men sought, however feebly, to express in glorious structures their conceptions of the beauty of holiness, and these works, our wonder, are but the outward and visible signs of the ideals which animated them.

To us in very different days life offers nearly the same problems, but the conditions have changed, and, as has happened before in the world's history, great material prosperity has weakened the influence of ideals, and blurred the eternal difference between means and end. Still, the ideal State, the ideal Life, the ideal Church—what they are and how best to realize them—such dreams continue to haunt the minds of men, and who can doubt that their contemplation greatly assists the upward progress of our race? We, too, as a profession, have cherished standards, some of which, in words sadly disproportionate to my subject, I have attempted to portray.

My message is chiefly to you, Students of Medicine, since with the ideals

entertained now your future is indissolubly bound. The choice lies open, the paths are plain before you. Always seek your own interests, make of a high and sacred calling a sordid business, regard your fellow creatures as so many tools of trade, and, if your heart's desire is for riches, they may be yours; but you will have bartered away the birthright of a noble heritage, traduced the physician's well-deserved title of the Friend of Man, and falsified the best traditions of an ancient and honourable Guild. On the other hand, I have tried to indicate some of the ideals which you may reasonably cherish. No matter though they are paradoxical in comparison with the ordinary conditions in which you work, they will have, if encouraged, an ennobling influence, even if it be for you only to say Rabbi Ben Ezra, "what I aspired to be and was not, comforts me." And though this course does not necessarily bring position or renown, consistently followed it will at any rate give to your youth an exhilarating zeal and a cheerfulness which will enable you to surmount all obstacles—to your maturity a serene judgment of men and things, and that broad charity without which all else is nought—to your old age that greatest of blessings, peace of mind, a realization, maybe, of the prayer of Socrates for the beauty in the inward soul and for unity of the outer and the inner man; perhaps, of the promise of St. Bernard, "*pax sine crimine, pax sine turbine, pax sine rixa.*"

A Technique of Bronchography in Children with Evaluation of Contrast Media

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Since 1947 an intensive study of endobronchial tuberculosis in children has been undertaken in the Chest Clinic of the Children's Medical Service of Bellevue Hospital.[1, 2] An attempt was made to determine by means of bronchography the incidence and types of residual bronchial and pulmonary disease in children previously found to have tuberculous endobronchial lesions on bronchoscopy. During 1955-56, 117 bronchograms were made in children with apparently healed endobronchial disease; in addition, seven bronchograms were carried out in children with non-tuberculous pulmonary disease, making a total of 124 bronchograms.

This investigation has provided an unusual opportunity to evaluate methods of bronchography in children, also three commonly used contrast media.

In recent years, bronchography has been used with greater frequency as an aid in the diagnosis and localization of pulmonary disease. However, its use in children has been limited, due to certain technical difficulties. Various methods for the introduction of the contrast medium have been used, such as supraglottic,[3] transglottic[4, 5] and subglottic[6] routes. Different techniques of anesthesia have been tried, using local anesthetics,[7] general anesthetics [3, 5] or a combination of both.[4, 8] Our satisfactory results in 110 out of 124 bronchograms (88 per cent) compare favorably with the other accurately reported series of bronchograms in children, namely that of Bates and his associates,[5] who obtained good bronchograms in 41 out of 50 cases (82 per cent) in 1950.

We attribute our good results particularly to the following factors: a) anesthesia, b) type and amount of contrast medium used, c) careful and systematic positioning of the patient following fractional instillation of the contrast medium, and d) radiographic technique.

Technique: The technique of bronchography described by Bates and his co-workers,[5] slightly modified by one of us (S.B.), has been used throughout the entire study.

Patients are admitted to the hospital on the day before bronchography and discharged on the following day. They are allowed a light breakfast but no lunch as the procedure is always performed between 1 and 3 p.m. When auscultation of the chest on admission reveals rales and rhonchi, the quality of the bronchograms is improved if postural drainage is performed for 10 minutes on the evening of admission and repeated the following morning.

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Scopolamine is given subcutaneously 30 to 60 minutes before the procedure. The dosage is 0.0002 Gm. for children up to six years of age and 0.0003 Gm. for older children. Occasionally Nembutal® by mouth in appropriate dosage is given to apprehensive or over-excited children.

Because the patients are in an age range of two to 13 years in this series, with one exception, a boy of 16 years (Table I), general anesthesia in the form of open-drop ether is used in all cases. When the patient reaches the second plane of anesthesia, direct laryngoscopy is performed and the largest possible endotracheal tube inserted and taped to the corner of the mouth opposite the side of the lung to be studied; secretions are aspirated through the lumen of the tube. Just prior to insertion of the endotracheal tube, its length is measured off on the fine rubber catheter (8-10 F.) which will be used for instillation of the contrast medium, and marked with a small strip of adhesive tape.

The patient is then taken to the radiographic room by the anesthetist.

Occasionally Cyclaine® solution has been sprayed directly into the endotracheal tube. Though it was obvious that this helped suppress the cough reflex better than general anesthetics alone, we feel that the danger of aspiration after the procedure is much greater than the benefit obtained from its use.

The catheter is introduced inside the endotracheal tube to the distance previously marked off, so that the contrast medium will be delivered at the end of the tube. The contrast medium is injected into the catheter with a 20 ml. syringe.

The total amount of contrast medium injected into each lung is approximately 1 ml. per year of age up to five years. A maximum of 8 ml. per lung is used for older children. The amount of contrast medium for each lung is divided as follows: for the *right* lung twice as much material is required for the lower lobe (first fraction) as for the middle (second fraction) and upper (third fraction) lobes together. In the case of the *left* lung, the amount for the lower lobe (first fraction) is the same, and half of this amount is divided between the lingula (second fraction) and the upper lobe proper (third fraction). For example, for a six year old child the total amount of material used for each lung is 6 ml.; 3 ml. are instilled into the lower lobe and 1.5 ml. each into the middle and upper lobes respectively on the right; on the left side, 3 ml. are instilled into

TABLE I

Age in Years	Number of Patients
2- 5	33
6- 9	44
10-13	22
16-	1
TOTAL	100

the lower lobe and 1.5 ml. *each* into the lingula and the left upper lobe proper. Each lobe is filled in turn after appropriate positioning of the patient.

Positioning of the Patient: A clear idea of the segmental anatomy of the lung is essential for satisfactory positioning. The segments of the lung are shown diagramatically in Figure 1 (segment 7 is not visualized on the right lateral view), numbered according to the scheme adopted by the International Committee in 1949.[9]

The order in which the segments are filled has been worked out with a view to minimizing the labor of moving the unconscious patient. Also it has been our experience that the quality of the bronchograms is better when the lower lobe bronchi are filled first, and those to the upper lobes just prior to radiography.

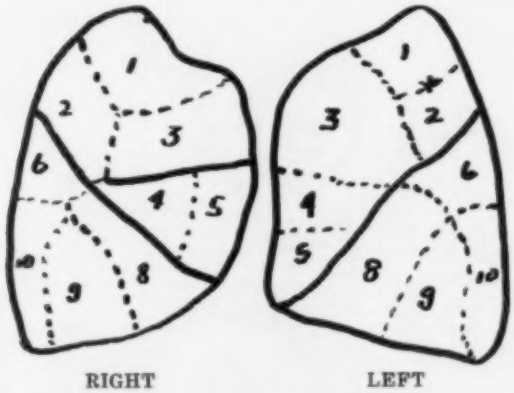
Good team-work is important. The assistant holds the child's head elevated, slightly hyperextended, and turned to the side opposite the lung to be studied. This helps to maintain the airway and to direct the flow of contrast medium to the side under study.

To outline each of the segments of the lung, the operator manipulates the patient successively in each of the six positions shown in Figure 2, all the while keeping the patient inclined (not rotated) towards the right side.

For outlining the bronchi to the *right* middle lobe (segments 4 and 5), the patient is placed in position 3; fraction 2 of the contrast medium is now instilled.

Fraction 3 of the contrast medium is instilled just after placing the patient in position 4; he is then turned to positions 5 and 6 respectively, leaving him 15 seconds in each position. This ensures complete filling of the apical, posterior and anterior segments of the right upper lobe (1, 2 and 3).

The above procedure ensures visualization of the right lung. For the *left* lung the entire sequence of positions is repeated as above, following instillation of fractions 1 and 2 of the contrast medium, the only difference



RIGHT LEFT

FIGURE 1: Lateral view of both lungs showing segmental distribution.

being that the patient is kept inclined (not rotated) towards the left. However, for fraction 3 he is placed on his left side (position 7) prior to instillation of the contrast medium, then rotated to the Trendelenburg positions 8 and 9.

Radiography: As soon as the contrast medium has been instilled and the child placed in the six positions, chest radiographs are taken in the following order:

Unilateral Bronchograms:	
	Lateral view.
	Posterior oblique view.
	Antero-posterior view.
Bilateral Bronchograms:	
Right Lung—	Right lateral view.
	Right posterior oblique view.
	Antero-posterior view.
Left Lung—	Left posterior oblique view.
	Antero-posterior view.

Ideally, respiratory movements should be eliminated when the radiographs are taken. However our experience has shown that the slight respiratory movements of the well-anesthetized child are compatible with excellent bronchograms. On several occasions, the endotracheal tube has been attached to a respiratory bag with a closed circuit so that the respira-

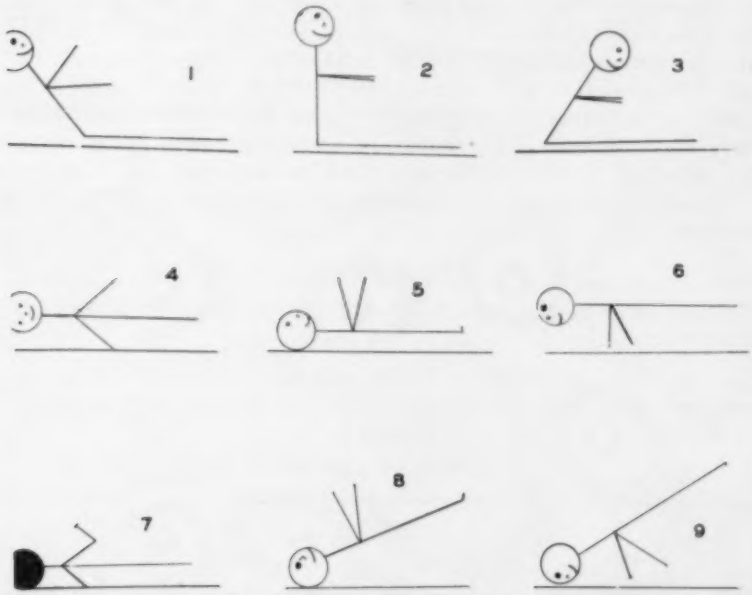


FIGURE 2: The patient is placed in position 1 just before instillation of fraction 1 of the contrast medium. This ensures flow of the medium to the apical segment of the right lower lobe. (6) The patient is left 15 seconds in this position and immediately placed in position 2 to ensure filling of the basal segments of the right lower lobe (7, 8, 9 and 10).

tions of the child could be controlled by the anesthetist during radiography; in this case radiographs are taken when the chest is inflated into the position of deep inspiration.

Recovery: After the radiographs are taken, the contrast medium is aspirated through the endotracheal tube. The child is then put in the position of postural drainage and returned to the ward as soon as he regains consciousness.

Complications: In this series of 124 bronchograms there was no case in which the underlying disease, tuberculous or non-tuberculous, appeared to be in any way aggravated by bronchography.

Two patients developed irritative conjunctivitis from ether anesthesia, with clearing within 48 hours.

Marked cyanosis developed in two patients as the contrast medium (Visciodol®) began to enter the second lung, although they had been asymptomatic throughout the first part of the procedure. Prompt recovery followed withdrawal of the material, suction, oxygen and postural drainage. The first patient was a six year old girl who had generalized pulmonary emphysema as well as extensive bilateral calcification of old tuberculous foci. The second patient was a five year old boy who previously had had active primary pulmonary tuberculosis and endobronchial lesions leaving him with bronchiectasis in the shrunken right middle lobe.

Enlargement of the thyroid gland occurred in a three year old boy, in whom three successive bronchograms were done at intervals of one to two months (September 22, 1955, November 27, 1955, and December 29, 1955). Lipiodol® was used on each occasion. The thyroid gland was noted to be enlarged on December 31, 1955 and the level of protein-bound iodine on January 31, 1956 was 27.6 gamma per cent (normal = 4-8 gamma per cent). By April 6, 1956 the thyroid gland had returned to almost normal size. The level of protein-bound iodine on September 2, 1956 was 10.4 gamma per cent.

Analysis of Bronchographic Results

A total of 124 bronchograms in 100 patients have been performed during the past year.

TABLE II

ALVEOLAR FILLING

	Lipiodol	Dionosil	Visciodol
Absent	10	12	22
Minimal	17	13	14
Moderate	10	14	4
Excessive	4	4	0
TOTAL	41	43	40

Three different contrast media have been used:

1. Lipiodol® (iodized oil, U.S.P.).
2. Dionosil® (propyliodone) aqueous suspension.
3. Visciodol® (lipiodol-sulfanilamide).

Criteria for Evaluation of Results of Bronchograms: Excellent Bronchograms: All segmental bronchi are well outlined; secondary and tertiary bronchi are well visualized; absence of or minimal alveolar filling, and good radiologic contrast.

Good Bronchograms: All segmental bronchi are adequately outlined; most of the secondary and tertiary bronchi are visualized; minimal to moderate alveolar filling, and adequate or fair contrast.

Adequate Bronchograms: Poor filling of the segmental bronchi which can, however, be traced; secondary and tertiary bronchi are poorly visualized; moderate to excessive alveolar filling without, however, obscuring the bronchial outline completely, and poor contrast.

Unsatisfactory Bronchograms: Incomplete filling of segmental bronchi which cannot be traced; excessive alveolar filling interfering with visualization of the bronchial outline, and poor contrast.

The details of our results with regard to alveolar filling and radiologic contrast can be seen in Tables II and III.

TABLE III

RADIOLOGIC CONTRAST

	Lipiodol	Dionosil	Visciodol
Good	20	13	37
Fair	16	14	3
Poor	5	16	0
TOTAL	41	43	40

TABLE IV

OVERALL RESULTS IN 124 BRONCHOGRAMS

Quality	Lipiodol	Dionosil	Visciodol
Satisfactory Excellent	4	3	22
Good	15	7	12
Adequate	15	27	5
Unsatisfactory	7	6	1
Total Number of Bronchograms	41	43	40
Total Number of Satisfactory	34	37	39

Discussion

We attribute the satisfactory results obtained in our bronchograms principally to: (a) the type of anesthesia; (b) the contrast medium, and (c) the careful and systematic positioning of the patient, and (d) radiographic technique.

(a) *Anesthesia:* Good anesthesia is the first essential for success in securing satisfactory bronchograms. In our series, open-drop ether anesthesia has proved to be the method of choice because of its simplicity and efficiency.

Inadequate anesthesia can be troublesome, giving rise to jerky respirations, coughing or even bronchospasm during instillation of the contrast medium. It may result in overfilling of the alveoli, motion during radiography and incomplete filling of the segmental bronchi.

(b) *Contrast Medium:* The contrast medium is important in obtaining successful bronchograms.

Lipiodol, an iodized oil, has been successfully used ever since its introduction by Sicard and Forestier in 1922.[10] We have performed 41 bronchograms in children using Lipiodol and find the main disadvantage to its use to be the delay in elimination of the material from the lung. As a result, the radiographic pictures remain obscured for many weeks or even months and repetition of bronchography becomes impossible. Another disadvantage is the ease of alveolar flooding, which can, however, be successfully prevented by proper manipulation. Postbronchographic collapse of portions of the lung reported by others[11] did not occur in our series. Clinical iodism, although rare, has been noted.[12, 13] One of our children developed enlargement of the thyroid gland with significantly prolonged eleva-

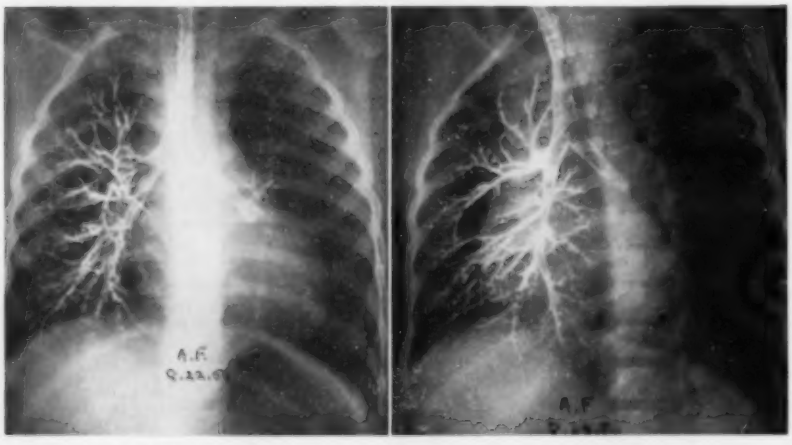


FIGURE 3A FIGURE 3B

Figure 3A: P-A view: Good normal bronchogram of right lung obtained with Visciodol.—*Figure 3B:* Right oblique view.

tion of the protein-bound iodine after three consecutive bronchograms. Hyde and Hyde[14] studied the blood iodine levels after administration of iodized oil and noticed high levels lasting many months after bronchography.

More recently, *Dionosil*, an organic iodine compound, suspended in water or peanut oil has been widely acclaimed as a more satisfactory contrast medium for bronchography.[15, 16] The advantage of using the aqueous suspension of Dionosil as the contrast medium has been demonstrated in 43 bronchograms. The main advantage over Lipiodol is the rapid absorption of the material which usually disappears from the lung within one week. This permits subsequent radiologic examination without interference by the contrast medium. We agree with others that, with the use of Dionosil, radiography can be unhurried, as the medium is slower in penetrating into the alveoli. The chief drawback to its use is the lack of sharp radiologic contrast. Furthermore, when alveolar filling does occur, it gives rise to blurring of the lung fields, thus enhancing the poor radiologic contrast produced by Dionosil. Dionosil will, however, give adequate results if the respiratory movements can be entirely eliminated during radiography, as in cooperative adults under local anesthesia, or in children when the respirations can be completely controlled by the anesthetist. Toxic reactions with Dionosil have been described,[15, 16] but did not appear in any of our patients.

A third contrast medium used in this study, *Visciodol*, is a suspension of sulfanilamide in iodized oil. This was accidentally discovered by Dormer, Friedlander, and Wiles[17] in 1945, and has been extensively used for bronchography especially in adults.[18] Visciodol in our experience has given the

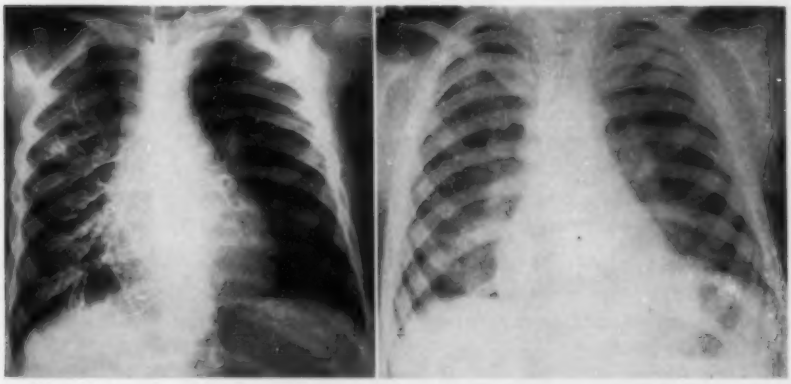


FIGURE 4A FIGURE 4B

Figure 4A: P-A view: Bronchogram obtained by instillation of Visciodol on August 29, 1956.—*Figure 4B:* P-A view of same patient on September 6, 1956 showing complete disappearance of contrast media.

most satisfactory results of the three contrast media employed. The bronchograms obtained are technically excellent (Figure 3A, B). Because of its high viscosity there is less tendency for the material to enter into the alveoli, thus allowing ample time for positioning of the patient and for unhurried radiography. Perhaps also because of its high viscosity, the material is more readily eliminated by the ciliary section of the bronchial mucosa and is not retained in the lung. We have taken follow-up radiographs within a week after bronchography and found no evidence of retained material (Figure 4A, B). Visciodol provided excellent radiologic contrast. Finally, in our own experience it lacks clinical toxicity from the iodized oil although we did find the protein-bound iodine fraction elevated in all cases studied to above 100 gamma per cent. The only unfortunate drawback of Visciodol is that the thickness of the material makes it troublesome to prepare: it needs constant warming and vigorous stirring up to the moment of use and even then it must be forcibly ejected from the syringe. Dangers from the use of too viscous a medium in outlining the bronchial tree have been stressed,[20] and from our experience with two patients described above, we believe it inadvisable to perform bilateral bronchograms simultaneously with Visciodol in children, unless the material is aspirated from the first side studied before proceeding to the second side.

(c) *Careful and Systematic Positioning of Patient:* Positioning of the patient is of utmost importance in obtaining complete filling of all of the segmental bronchi of the lung. It is also important to instill the contrast medium by the fractional method described above. This technique assures the proper distribution of the opaque material in all segments of the lung.

(d) *Radiographic Technique:* The final success of bronchography really depends upon the radiographic pictures obtained. Naturally, the best possible technique will give the best results.

SUMMARY

One hundred and twenty-four bronchograms were performed in 100 children; 110 of these bronchograms were satisfactory. Our experience leads us to believe that successful bronchography in children depends upon the anesthesia, the choice of contrast material, careful positioning of the patient to ensure complete filling of all segmental bronchi and finally upon the radiographic technique. Our exact technique is described in detail, as well as the advantages and disadvantages of three contrast media, namely, Lipiodol, Dionosil and Visciodol.

The patient is admitted to the hospital for the procedure; postural drainage is instituted prior to anesthesia if physical examination reveals presence of rales. Scopalamine followed by open drop ether is the method used. Direct laryngoscopy permits insertion of an endotracheal tube, and the contrast material is inserted through a catheter of known length. Most satisfactory results have been obtained using Visciodol (sulfanilamide in iodized oil). For best results it is advised that this material be warmed and vigorously stirred up to the moment of instillation. Exact amounts of contrast material and sequence of positions are described in the text.

Better than 85 per cent satisfactory bronchograms have been obtained using this method.

Untoward reactions have been noted: cyanosis may occur if both lungs are done simultaneously with Visciodol; aspiration of the first side before proceeding to the second side is therefore recommended. High iodine levels and enlargement of the thyroid following the use of Lipiodol and Visciodol have been noted by others as well as by ourselves.

ACKNOWLEDGMENTS

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Dr. Herbert Kupperman of New York University College of Medicine has kindly determined the protein-bound iodine levels.

One of us (S. B.) is indebted to Parke, Davis and Company for a financial grant enabling him to complete the study.

We are grateful to E. Fougera and Company, Incorporated, for supplying the Visciodol used in this study.

RESUMEN

Se hicieron ciento veinticuatro broncogramas en 100 niños; 110 de ellos fueron satisfactorios. Nuestra experiencia nos lleva a creer que la broncografía bien lograda depende en los niños, de la anestesia, la elección del medio de contraste, la posición cuidadosa del enfermo para asegurar el llenado completo de todos los bronquios segmentarios y por último también depende de la técnica radiográfica. Se describe nuestra técnica con exactitud en detalle así como las ventajas y desventajas de los medios de contraste como son: lipiodol, dionosil y visciodol.

El enfermo ingresa al hospital para el procedimiento; se hace primero drenaje postural, antes de la anestesia si la auscultación revela estertores. Se usa la escopolamina seguida de la anestesia al éter por goteo abierto. La laringoscopía permite la inserción del tubo endotraqueal y el medio de contraste se inyecta a través de un cateter de longitud conocida. Los mejores resultados se obtienen con visciodol (sulfanilamida en aceite yodado). Para obtener mejores resultados se aconseja que este material se caliente y se agite vigorosamente hasta el momento de la instilación.

Se describen las posiciones que deben usarse y las cantidades exactas de medios de contraste. Más del 85 por ciento de resultados satisfactorios se logran por este método.

Reacciones desagradables que se han observando: cianosis puede ocurrir si los dos pulmones se instilan con visciodol; la aspiración del primer lado antes de emprender el segundo se recomienda.

Elevadas concentraciones de yodo y crecimiento de la glándula tiroides después del lipiodol o del visciodol se han notado por otros así como por nosotros.

RESUME

124 bronchogrammes ont été obtenus chez 100 enfants. 110 de ces bronchogrammes furent satisfaisants. L'expérience des auteurs les conduit à penser qu'une bronchographie satisfaisante chez les enfants dépend de l'anesthésie, du choix de la substance de contraste, de la position convenable du malade pour obtenir la pénétration complète de toutes les bronches segmentaires, et finalement de la technique radiographique. La technique précise des auteurs est décrite en détail, ainsi que les avantages et les inconvénients de trois substances de contraste, à savoir: le lipiodol, le dionosil, et le visciodol.

Le malade est admis à l'Hôpital pour cet examen; un drainage de posture est institué avant anesthésie si l'examen physique révèle la présence de râles. Les auteurs utilisent la méthode d'anesthésie par la "scopalamine" suivie par l'administration d'éther. La laryngoscopie directe permet l'insertion du tube endotrachéal, et la substance de contraste est instillée par un cathéter de longueur connue. La plupart des résultats satisfaisants ont été obtenus par la visciodol (sulfanilamide dissous dans de l'huile iodée). Pour obtenir les meilleurs résultats, il est conseillé de chauffer cette substance et de l'agiter vigoureusement au moment de l'instillation. Les quantités exactes de substance de contraste et les positions sont décrites dans le texte. Plus de 85% des bronchogrammes satisfaisants ont été obtenus par cette méthode.

Des réactions secondaires ont été notées: de la cyanose peut survenir si les deux poumons sont instillés en même temps par le visciodol; l'aspiration du premier côté avant de procéder à l'instillation du deuxième est dés lors recommandée. Les auteurs comme d'autres l'avaient déjà signalé, ont noté un taux élevé d'iode, et l'augmentation de la thyroïde après emploi du lipiodol et du visciodol.

ZUSAMMENFASSUNG

Es wurden 124 Bronchogramme an 100 Kindern vorgenommen; 110 von diesen Bronchogrammen waren befriedigend. Unsere Erfahrung veranlasst uns zu der Überzeugung, dass eine erfolgreiche Bronchografie bei Kindern unabhängig ist von der Anaesthesie, der Wahl des Kontrostmittels, sorgfältiger Lagerung des Patienten, um eine komplette Füllung aller Segmente und Bronchien zu gewährleisten, und schliesslich von der Röntgen-Technik. Unsere exakte Technik wird in den Einzelheiten beschrieben, ebenso wie die Vorzüge und Nachteile der 3 Kontrastmittel, nämlich Lipiodol, Dionosil und Visciodol.

Der Patient wird für den Eingriff im Krankenhaus stationär aufgenommen; eine Lagedrainage wird durchgeführt vor der Anaesthesie, sofern die physikalische Untersuchung des Bestehen von Rasselgeräuschen ergibt. Scopalomin mit anschliessendem Tropf-Aether ist das angewandte Verfahren. Direkte Laryngoscopie ermöglicht die Einführung eines endotrachaealen Tubus, und das Kontrastmittel wird durch einen Katheder bekannter Länge eingeführt. Das am meisten befriedigende Resultat wurde erzielt bei der Verwendung von Visciodol (Sulfanilamid in Jod-

Öl). Um die besten Resultate zu gewinnen, wird emfohlen, dieses Material zu erwärmen und kräftig zu schütteln bis zu dem Augenblick der Einfüllung. Exakte Mengenangaben des Kontrast materials und die Reihenfolge der Lagerung werden im Text beschrieben. Mehr alse 85% befriedigende Bronchogramme wurden unter Verwendung dieser Methode erzielt.

An Nebenwirkungen kamen zur Beobachtung: Es kann eine Blausucht auftreten, wenn beide Lungen gleichzeitig mit Visciodol gefüllt werden; eine Absaugung der ersten Seite wird daher empfohlen, bevor man zur Darstellung der anderen Seite übergeht. Hohe Jodspiegel und Vergrosserung der Schilddrüse nach dem Gebrauch von Lipiodol und Visciodol sind so wohl von anderen Autoren, als auch von uns selbst beobachtet worden.

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Ballistocardiography: Concepts of its Applicability in the Office Practice of Cardiology

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Ballistocardiography itself cannot rightly be called a new procedure, however the clinical application of the method must be so considered. The movements recorded by Isacc Starr[1] in 1939, when he introduced the term "ballistocardiogram," had already been known for some 75 years. From the clinician's standpoint, much is owed to Starr for his contributions in this field. He pointed out many of the physiologic events concerned in the evolution of the ballistocardiogram, devised formulas for estimating cardiac output, and initiated clinical studies with the ballistocardiograph.[2]

As with any "new" method, there are those who are prone to look at ballistocardiography as being essentially an empiric method and to decry its acceptance into the armamentarium of diagnostic studies. There are others who tend to go to the opposite extreme and extoll its virtues as a *sine qua non* in the study of cardiovascular disease. Naturally, there would follow an intermediate group which weighs the evidence pro and con, both from reports in literature and from their own clinical observations. From the numerous publications on the subject during the past decade, particularly those dealing with the clinical applications, it would appear that ballistocardiography does have a definite place in the study of cardiovascular disease, more specifically, coronary artery disease. The Mandelbaums[3, 4] found that 200 of 224 patients with clinical angina pectoris had abnormal ballistocardiograms. Moser and associates[5] obtained abnormal ballistocardiograms in about 80 per cent of patients with previous myocardial infarction (three weeks to 12 years after acute episodes); tracings were normal in about 20 per cent of the cases regardless of age. In patients with angina pectoris following coronary occlusion a normal ballistocardiogram was found by these investigators in only 7 per cent. Taymor and associates[6] found the resting ballistocardiogram abnormal in 83 per cent of 75 patients with angina pectoris who had normal resting electrocardiograms and positive Master's two step tests; after exercise the tracings became abnormal in an additional eight patients, making the ballistocardiogram abnormal in 93 per cent of these individuals. Brown[7] in a series of over 55 patients with myocardial infarction found no normal tracings.

This report, which reaffirms the observation that the most marked variations from the normal pattern to be found in ballistocardiography are those exhibited by individuals suffering from coronary artery disease and accompanying myocardial damage,[8] deals with impressions formed

FIGURE 1: Abnormal ballistocardiogram on S. A. S. six weeks before acute myocardial infarction showing increased height of the H waves and decreased amplitude of the J waves, constituting the "early M" pattern. There is also increased respiratory variation. After smoking the H wave components are further exaggerated.

after reviewing over 400 ballistocardiograms performed on 286 private patients and patients referred from the local Veterans Administration Hospital during a three year period (1953-1956). The tracings were obtained on a high-frequency Starr-type ballistocardiograph attached to a twin channel recorder, permitting simultaneous inscription of electrocardiograms and ballistocardiograms. It has become increasingly apparent from this study that the primary applications of this method to clinical cardiology lie in the objective documentation of coronary artery disease and evaluation of myocardial damage. Its use in a wide variety of other cardiovascular disease entities appears to be superfluous and is surpassed by more conventional methods. Four distinct areas for the use of ballistocardiography in clinical cardiology stand out: 1) detection of the "prodromal stage" of acute myocardial infarction; 2) appraisal of the functional recovery of the heart muscle following acute myocardial infarction; 3) objective documentation of old myocardial infarction in the presence of normal electrocardiograms when records made during the acute phase are not available; 4) evaluation of the significance of paroxysmal rapid heart action and ectopic beats.

"Prodromal Stage" of Myocardial Infarction

The following case summaries are presented to illustrate the use of ballistocardiography in the detection of impending myocardial infarction when the studies usually employed show no abnormalities.

S. A. S., a 48 year old white physician with a family history of hypertension and coronary heart disease, noticed in October, 1955, that pulling his golf cart brought on anterior chest pain, which was relieved by resting a few minutes. He subsequently

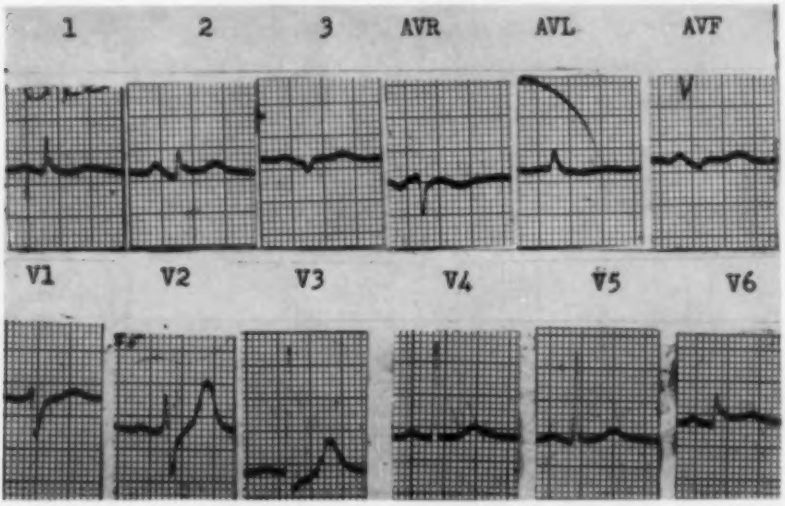

FIGURE 2: Typical changes of acute postero-lateral myocardial infarction are evident in the electrocardiogram of S. A. S. obtained shortly after hospitalization.

experienced similar pain while walking or working in his garden. Sublingual nitroglycerine caused flushing of the face but did not shorten the pain. Several resting electrocardiograms were normal, as were Master's two step tests. A definitive diagnosis could not be made, and he was allowed to continue his usual activities. On November 4, 1955, a resting ballistocardiogram was found to be grossly abnormal, and the complexes showed further deterioration after smoking (Fig. 1). On December 28, 1955, he developed severe, knife-like, substernal pain with radiation down the ulnar aspect of both forearms and was hospitalized at the Veterans Administration Hospital. On admission he was pale and was sweating profusely; physical examination was otherwise non-contributory. The pain lasted approximately 24 hours. Pertinent laboratory findings were white blood cell count of 25,800 and erythrocyte sedimentation rate of 30 mm. in one hour. X-ray film of the chest was normal. The electrocardiogram (Fig. 2) was compatible with acute postero-lateral myocardial infarction. He was discharged after 30 days under conventional management.

D. L. P., a 44 year old white mechanic, was admitted to the Veterans Administration Hospital November 7, 1954, because of precordial and left arm pain. He had been well until two weeks prior to admission, at which time he became unduly exhausted while tending livestock. That night, while at a drive-in theater, he developed precordial pain with radiation to the left shoulder and arm. He got out of the car and walked around; the pain disappeared after three or four minutes. From then until the time of admission he experienced one to several such attacks daily, coming on either at rest or upon exercise and lasting from four to 20 minutes. The clinical impression on admission to the hospital was coronary artery disease. Physical examination was essentially negative, and laboratory findings were normal. He continued to have two or three attacks of chest and arm pain daily, coming on at rest and lasting 10 to 15 minutes; the location of the pain varied from the left scapula to the left hand and precordium. Sublingual nitroglycerine gave questionable relief from two attacks but on the whole was not effective. An electrocardiogram November 16, 1954, showed no significant change from the previous tracing. The lack of objective findings created doubt concerning the accuracy of the initial impression. Ballistocardiographic studies were recommended and were performed November 19, 1954. While he was lying quietly on the table free of chest pain the ballistic complexes were of good amplitude and easily identifiable. During the tracing the patient complained of severe chest pain, and the complexes became decreased in amplitude, difficult to identify and generally chaotic; the H waves increased in height and the J waves diminished, constituting the

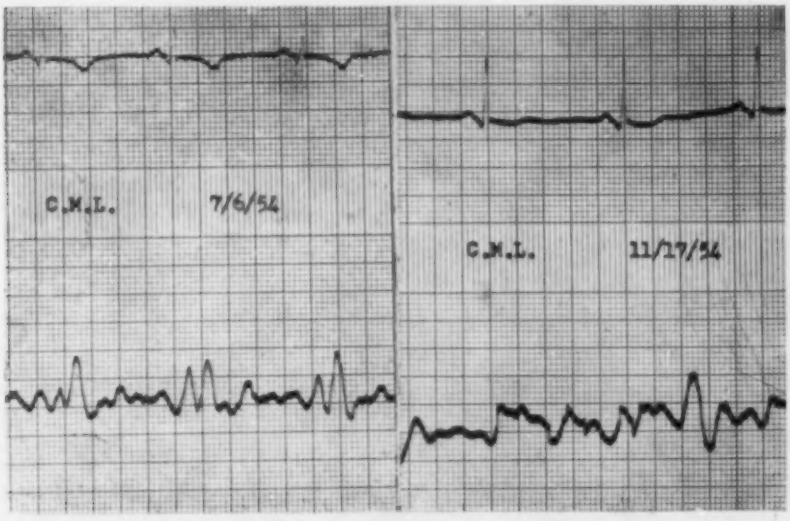

FIGURE 3A FIGURE 3B

Figure 3A: Ballistocardiogram obtained during the initial examination of C. M. L. —*Figure 3B:* Obtained four months later and shows marked deterioration (see text).

"early M" pattern. Three minutes after administration of 0.4 mgm. nitroglycerine sublingually the pain disappeared, and the ballistic complexes became completely normal. These findings, along with the clinical picture, prompted the diagnosis of coronary artery disease with probable impending infarction. Treatment consisting of bed rest and Dicumarol® was instituted November 19, 1954. The attacks gradually subsided, and he became pain-free December 6; the Dicumarol® was discontinued December 14. He remained asymptomatic until December 21 (approximately 60 days after the initial onset of pain), when he developed severe anterior chest pain, dyspnea and orthopnea, accompanied by electrocardiographic changes characteristic of acute postero-lateral myocardial infarction. Dicumarol® was reinstituted and conventional treatment for heart failure prescribed. An uneventful recovery ensued.

Comment: In the face of normal electrocardiograms and exercise tests, the attacks of chest and arm pain created a dilemma in these two patients. The ballistocardiographic abnormalities represented the first objective evidence of coronary artery disease, and, coupled with the subjective complaints, suggested the premonitory syndrome of acute myocardial infarction. The validity of this hypothesis is substantiated by the recorded course of events in both instances.

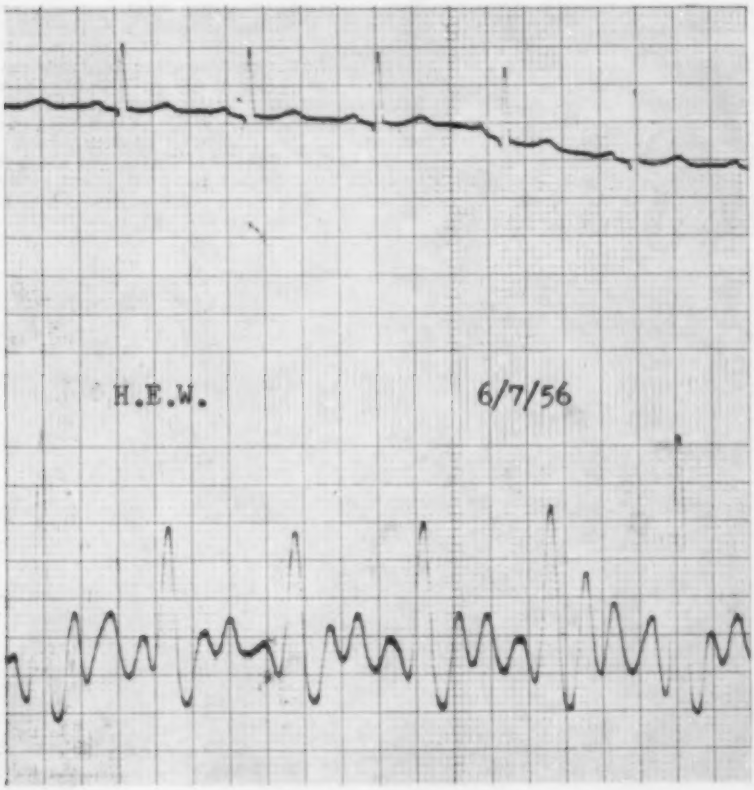

FIGURE 4: Normal ballistocardiogram of H. E. W. 10 months after acute myocardial infarction.

Functional Recovery Of The Heart Muscle Following Acute Myocardial Infarction

The use of ballistocardiography in appraising the functional recovery of the heart muscle following acute myocardial infarction has been recommended[9] and has been found by this observer to be a reliable yardstick with respect to prognosis. The following cases are cited as examples.

C. M. L., a 51 year old white engineer, was first examined in my office July 6, 1954. He stated that he had been hospitalized at the Veterans Administration Hospital May 26, 1954, because of a "heart attack." He signed out of the hospital against advice five weeks after admission (April 28). The following day he had a short bout of left antero-lateral chest pain, which was relieved by an injection given by his physician; the next day the same discomfort abated following two nitroglycerine tablets sublingually. During and after his hospital stay he had noted high substernal burning sensations, particularly after the evening meal. The entire physical examination performed by me revealed no abnormality with the exception of slightly increased sheathing of the retinal arteries and some AV compression. Fluoroscopy revealed the left ventricle to be moderately enlarged, chiefly in the inflow tract. The electrocardiogram showed typical evolutionary changes of acute antero-septal myocardial infarction. The ballistocardiogram was grossly abnormal in that all complexes were decreased in amplitude and the typical "early M" pattern was present (Fig. 3A). He was observed over the ensuing five months, and, in spite of essentially bed to chair existence, he continued to have frequent attacks of substernal burning. Repeated electrocardiograms were unchanged from the initial record. Serial ballistocardiograms showed progressive deterioration to the extent that the records became chaotic and the individual complexes unidentifiable (Fig. 3B). He died suddenly in January, 1955, shortly after moving to North Carolina. No autopsy was performed.

H. E. W., a 44 year old white electrician, suffered an acute myocardial infarction in August, 1955, and was referred by his company physician for cardiovascular evaluation June 7, 1956. Physical examination revealed no abnormalities, and fluoroscopy of the chest showed the heart and great vessels to be well within the limits of normal. Typical evolutionary changes of acute anterior wall myocardial infarction were present in serial electrocardiograms done while he was hospitalized. The electrocardiographic tracing obtained June 7, 1956, was interpreted as being within the limits of normal, as was the ballistocardiographic record (Fig. 4).

Comment: The progressive deterioration of the ballistic complexes in C.M.L. with stationary electrocardiographic changes paralleled the downhill course. The entirely normal ballistic tracing on H.E.W. 10 months after the acute infarct was compatible with what apparently was a remarkable functional recovery of his myocardium.

Old Myocardial Infarction

Confirmation of old myocardial infarction in the presence of normal electrocardiograms is illustrated by the following case.

H. H., a 50 year old white merchant, was seen July 21, 1953. In April of that year he experienced an attack of left anterior chest pain which lasted several hours and disappeared. He was told by his physician that he had suffered a heart attack and was kept at bed rest at home for about two weeks. He stated that he had been a known hypertensive for several years but since that episode he had been normotensive, a fact borne out by finding the blood pressure to be 120-130/80. He had remained free of chest pain since the attack and had no symptom referrable to the cardiovascular system. There were no abnormalities on physical examination and chest fluoroscopy; his electrocardiogram (Fig. 5A) was essentially normal. Definite "early M" patterns were seen in the ballistocardiogram (Fig. 5B).

Comment: On the basis of electrocardiograms such as found in this man it would be difficult to substantiate the past occurrence of myocardial infarction. The needed objective evidence of cardiac disease in this situation is often furnished by ballistocardiographic study. This may be particularly significant when electrocardiograms were not done during the acute attack or are not available.

Paroxysmal Rapid Heart Action and Ectopic Beats

On the basis of the observations of Selinger and Levin[10] there would appear to be correlation between ballistocardiographic findings and the presence or absence of organic heart disease in cases of paroxysmal rapid heart action, but to date there have been few other publications concerning this correlation. The potential value of ballistocardiography in this area is further illustrated by the following case summaries.

E. R., a 42 year old white woman, was referred August 31, 1956, because of arterial hypertension and occipital and right frontal headaches of six years' duration. At the time of examination she was complaining of occipital headache, nausea and vomiting, and marked weakness; otherwise, she was asymptomatic. During the examination she volunteered the information that an unhappy marriage had ended in divorce in 1947 and that she had been caring for her chronically ill mother while working for a living under "nerve-racking" circumstances. Her blood pressure was 130/80-90 in both arms; 124/90 in the legs. Physical examination was otherwise not remarkable with the exception of regular tachycardia with apical and radial rates of 150/min. The electrocardiogram was abnormal in that a supraventricular tachycardia with a ventricular rate of 150/min. was present. She was hospitalized immediately, and four hours after rapid oral digitalization a normal sinus rhythm was restored (confirmed electrocardiographically); however, it was interrupted by frequent premature ventricular contractions. The blood pressure rose to and stabilized at 180-190/100-110 in both arms. On September 11 she was readmitted to the hospital for evaluation of her hypertension. All studies, including chest x-ray films, intravenous pyelogram, and renal function tests, were normal. Tests for pheochromocytoma were also normal. A ballistocardiogram was done September 14, and the tracing was well within the limits of normal. The electrocardiogram still showed the presence of normal sinus rhythm with frequent premature ventricular contractions.

S. E., a 46 year old white man, was referred by his physician for hospitalization November 29, 1954, because of intractable tachycardia. He gave a history of recurrent bouts of rapid heart action for the past 25 years; the attacks started and ended abruptly and usually lasted only a few minutes. Such maneuvers as holding a deep inspiration, gagging, belching, or drinking cold beverages had been effective in terminating the attacks; however, he recalled an episode two years previously which did not respond to these measures, and he was treated successfully with quinidine sulfate. The present bout had begun three days prior to examination when he turned suddenly in bed and had proved refractory to all previously successful measures. On examination the blood pressure was 110/?. The pulse rate was rapid and difficult to count; the apical

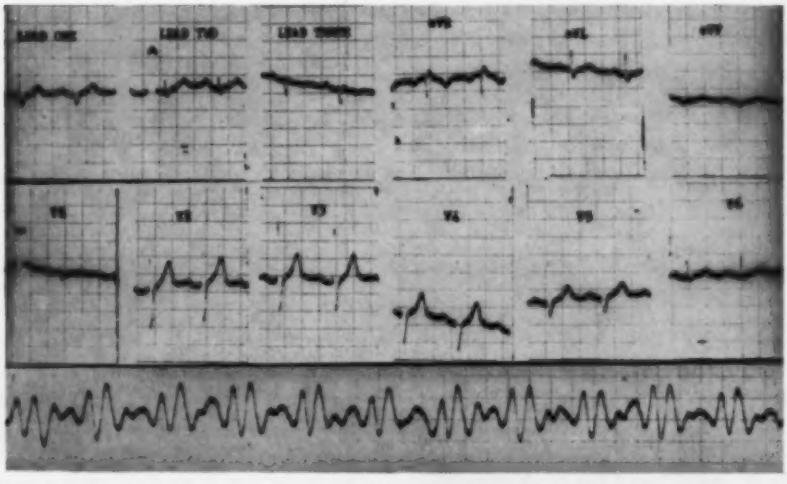

FIGURE 5A

FIGURE 5B

Figure 5: Normal electrocardiogram (*A*) and abnormal ballistocardiogram showing "early M" pattern (*B*) of H. H. three months after acute myocardial infarction.

rate was regular and ranged between 180-200/min. The electrocardiogram revealed supraventricular tachycardia (paroxysmal atrial tachycardia) with regular ventricular rate of 200/min. Two hours after the initial dose of Digoxin,® a modified Valsalva maneuver resulted in prompt reversion of the ectopic rhythm to normal sinus rhythm with atrial and ventricular rates of 80/min. The electrocardiogram became normal except for digitalis effect. A ballistocardiogram November 30, 1953, was grossly abnormal in that there was a markedly increased respiratory variation with many "early M" patterns. Reports from the referring physician after he returned to his home indicated that the attacks were increasing in frequency and severity in spite of all therapeutic measures.

Comment: The normal ballistocardiogram in the case of E.R. was believed to indicate absence of significant heart damage, while the abnormal tracings on S.E. suggested myocardial derangement. In the latter case the increased frequency of attacks and subsequent resistance to treatment would be in keeping with the abnormal ballistocardiogram.

Discussion

The principal ballistic abnormalities seen in symptomatic coronary artery disease have been described by Starr,[8] Brown and associates,[7] Gubner,[11] and others. Essentially these changes consist of increased respiratory variation, irregular and indefinite pattern, decreased amplitude of the IJ segments, notched J waves, and "early M" pattern (prominent H and L waves, low I and J segments). By far the most consistent abnormality seen in this study in the presence of advanced coronary artery disease has been the "early M" pattern. Although the other aberrations listed have also been observed, the "early M" pattern has occurred so frequently that it has been tempting to consider it pathognomonic of coronary artery disease. It might be mentioned that those patients in whose tracings the "early M" pattern persisted with good amplitude of the constituent waves, as illustrated by S.A.S. and H.H., have fared much better than those whose records became chaotic and remained so, for example, C.M.L.

Several statistical studies have been reported[12, 13 14] since Dock commented on the ballistic deterioration attributable to smoking in 1951.[15] Although the explanation for the reaction is not clear, it would appear that the "cigarette test"[14] has a certain degree of diagnostic value. The test involves having the subject smoke a standard brand cigarette at his usual rate after a basal ballistocardiogram and repeating the tracing five minutes afterwards. The test is considered positive only when there is definite deterioration in the majority of the ballistic complexes after smoking. It offers little inconvenience except in non-smokers and was employed routinely in cases of suspected coronary artery disease. It has been interesting to note the frequency with which ballistocardiograms of patients with coronary artery disease deteriorate after smoking, in contrast to the lack of change in "normal" subjects.

Ectopic beats and arrhythmias, particularly supraventricular tachycardias, occur in structurally normal hearts as well as in hearts that are structurally abnormal. Quite often the history is non-contributory, and conventional diagnostic procedures reveal no abnormality. In such instances it is usually assumed that no organic heart disease is present, but the need for a more accurate appraisal of the presence or absence of myo-

cardial damage is recognized. It would appear that ballistocardiography is at least a forward step in this direction. In the presence of supraventricular tachycardia, reliance on the ballistic record obviously should be delayed until normal sinus rhythm is restored; this is not necessary in cases manifesting only ectopic beats. The ballistic changes seen in abnormal records on these patients are essentially those found in those with myocardial damage secondary to coronary artery disease. There have been a number of such records obtained, but conclusive evidence for this means of differentiation is lacking at the present time since none in this category has come to necropsy.

The most serious deterrent to the infallibility of ballistocardiography is the effect of aging. While it is generally agreed that most clinically normal persons below the age of 50 have normal ballistocardiograms, a significantly large percentage of individuals beyond this age who have no cardiovascular complaints have abnormal ballistic tracings.[16] Nevertheless, symptomatic coronary artery disease does exist in a large number of patients under the age of 50 in the absence of abnormalities in routine studies such as physical examination, cardiac fluoroscopy, chest x-ray film, 12 lead resting electrocardiograms and "stress tests."[14, 17, 18, 19] Ballistocardiography is indicated in such instances, and abnormal records do offer objective evidence of coronary artery disease. Normal records can be obtained in the "young" age group with coronary artery disease and healed myocardial infarction,[16] as in the case of H.E.W., however this occurred infrequently in this study.

These observations would support Starr's tenet that "the ballistocardiograph is a physiological instrument designed to make readily available to clinicians information about certain fundamental aspects of the heart's function, especially its strength or weakness."[20] If the limitations of the method are recognized, its value as an ancillary tool in the study of coronary artery disease can be properly appreciated.

SUMMARY

1. Four distinct areas for the use of ballistocardiography in clinical cardiology became apparent after reviewing over 400 ballistocardiograms obtained during a three year period. These applications are presented under descriptive headings with illustrative case summaries.
   A. Ballistocardiography is of definite value in the detection of impending myocardial infarction when the studies usually employed show no abnormality.
   B. The method was found to be valuable in appraising the functional recovery of the heart muscle following acute myocardial infarction. Normal records would seem to indicate a good prognosis; progressive deterioration of the complexes in the presence of stationary electrocardiographic changes paralled poor clinical courses.
   C. Abnormal ballistocardiograms often furnish needed objective evidence of myocardial damage when the past occurrence of myo-

cardial infarction can not be substantiated by conventional methods and records made during the acute phase are not available.

D. Ballistocardiography has potential value in the evaluation of ectopic beats and paroxysmal rapid heart action. Further investigation of this method in such cases is definitely warranted.

2. The most consistent abnormality found in the presence of advanced coronary artery disease was the "early M" pattern.
3. The effect of cigarette smoking on ballistocardiograms in cases of suspected coronary artery disease further helps to determine the presence or absence of the entity ("cigarette test").
4. The most significant limitation of ballistocardiography found in this study was the effect of aging. However, abnormal records do offer objective evidence of coronary artery disease in patients under the age of 50 years who present no abnormality on physical examination, cardiac fluoroscopy, chest x-ray, 12 lead resting electrocardiograms and "stress tests."

RESUMEN

1. Existen cuatro ind.caciones claras para el uso de la balistocardiografía según ha sido aparente después de revisar más de 400 balistocardiogramas obtenidos en tres años:
   A. La balistocardiografía es de valor definido en la valuación y descubrimiento de un infarto cardiaco inminente, en tanto que los estudios habitualmente empleados no revelan anormalidad.
   B. Es de valor para estimar la recuperación funcional del músculo cardiaco después de un infarto agudo del miocardio. Los récords normales parecerían indicar unbuen pronóstico; el deterioro progresivo de los complejos en presencia de alteraciones electrocardiográficas estacionarias son paralelos a mala evolución.
   C. Los balistocardiogramas anormales a menudo necesitaron evidencia ulterior de daño al miocardio cuando la ocurrencia de infarto previo no puede asegurarse por métodos habituales y los récords hechos durante la faseaguda no se tienen a mano.
   D. La balistocardiografía tiene un valor potencial en la estimación de los latidos ectópicos y en caso de acción cardiaca rápida y paroxísmica. Astá justificada la investigación ulterior de este método en tales casos.
2. La anormalidad más consistente que se encontró en presencia de enfermedad avanzada de la arteria coronaria, fué el aspecto "precoz M."
3. El efecto de fumar cigarrillos sobre los balistocardiogramas en casos de sospecha de enfermedad coronaria, ayuda además para determinar la presencia o ausencia de la entidad ("Prueba del cigarrillo").
4. La limitación más significante de la balistocardiografía encontrada en este estudio fué el efecto de la edad. Sin embargo, los récords anormales ofrecen una evidencia objetiva de la enfermedad coronaria en enfermos debajo de 50 años quienes no presentan anormalidad al examen físico, a la cardio-fluoroscopia, a la radiografía de torax, a los

electrocardiogramas en reposo con 12 derivaciones y a las "pruebas de esfuerzo" (Stress tests).

RESUME

1. On peut discerner quatre domaines distincts dans l'emploi de la ballistocardiographie en cardiologie clinique. Telles sont les conclusions d'une étude de 400 ballistocardiogrammes obtenus pendant une observation portant sur un délai de trois ans. Ces notions sont présentées de manière descriptive avec les résumés des cas démonstratifs:
   A. la ballistocardiographie est de grande valeur pour détecter l'infarctus myocardique menaçant, alors que les moyens habituellement employés ne montrent aucune anomalie;
   B. la méthode est susceptible de mettre en lumière la guérison fonctionnelle du muscle cardiaque après l'infarctus myocardique aigu. Les tracés normaux sembleraient indiquer un bon pronostic; la détérioration progressive des complexes tandis que les altérations électrocardiographiques sont invariables font augurer une évolution clinique de mauvais pronostic;
   C. les ballistocardiogrammes anormaux fournissent souvent la preuve objective recherchée d'altérations myocardiques quand l'existence d'un ancien infarctus myocardique ne peut être affirmée par les méthodes conventionnelles et que les constatations faites pendant la période aiguë ne sont pas valables;
   D. la ballistocardiographie a une valeur certaine dans l'estimation des battements ectopiques et des crises de tachycardie paroxystique. Une étude ultérieure de cette méthode est vivement désirable dans de tels cas.
2. L'anomalie la plus importante trouvée dans les atteintes graves de l'artère coronaire a été le dessin "précoce en M."
3. L'effet de la fumée de cigarette sur les ballistocardiogrammes lorsqu'on soupçonne une affection de l'artère coronaire permet de determiner ultérieurement la présence ou l'absence de cette atteinte ("test de la cigarette").
4. La limitation la plus importante de la valeur de la ballistocardiographie trouvée dans cette étude a été due à l'effet du vieillissement. Cependant, des tracés pathologiques offrent la preuve objective d'atteinte de l'artère coronaire chez des malades âgés de moins de 50 ans, qui ne présentent aucune anomalie à l'examen physique, à la radioscopie cardiaque, à l'examen radiographique du thorax, sur les électrocardiogrammes et lors des tests.

ZUSAMMENFASSUNG

1. Vier bestimmte Gebiete für die Benutzung der Ballistocardiographie im Rahmen der klinischen Cardiologie haben sich ergeben nach der Durchsicht von 400 während eines Zeitraumes von 3 Jahren gewonnenen Ballistocardiogrammen. Diese Anwendungsgebite werden aufgeführt mit beschreibenden Leitsätzen und erläuternden Zusammenfassungen von Krankheitsfällen:

A. Die Ballistocardiographie ist von bestimmten Wert bei der Feststellung eines drohenden Herzinfarktes, wenn die gewöhnlich angewandten Untersuchungen keine Abweichungen zeigen.

B. Die Methods erwies sich als von Wert bei der Abschätzung der funktionellen Erholung des Herzmuskels im Anschluss an einen akuten Myocard-Infarkt. Normal Befunde würden eine gute Prognose anzuzeigen scheinen; fortschretende Verschlechterung der Komplexe bei Vorliegen stationärer elektrocardiographischer Veränderungen gingen parallel mit schlechten klinischen Verläufen.

C. Abnorme Ballistocardiogramme liefern oft die benötigte objektive Evidenz eines Myocard-Schadens, wenn das frühere Vorkommen eines Myocardinfarktes durch die konvensionellen Methoden nicht bewiesen werden kann und während de akuten Phase angefertigte Aufzeichnungen nicht zur Verfügung stehen.

D. Die Ballistocardiographie hat einen potentionellen Wert bei der Auswertung verlagerter Herzschläge und paroxysmal beschleunigter Herzaktion. Weitere Untersuchung mit dieser Methode in solchen Fällen ist sicher gerechtfertigt.

2. Die am meisten übereinstummende Abweichung von der Norm, die bei Vorliegen fortgeschrittener Coronararterienerkrankung gefunden wurde, war der "frühe M"—Typ.

3. Die Wirkung des Zigarettenrauchens auf Ballistocardiogramme bei Fällen mit verdächtiger Coronararterienerkrankung ist eine weitere Hilfe bei der Feststellung des Vorliegens oder Fehlens der Hauptkrankheit ("Zigarettentest").

4. Die am meisten bedeutsame Leistungsgrenze der Ballisticardiographie, die sich bei dieser Untersuchung ergab, war der Einfluss des Alters. Es ergeben jedoch abnormale Befunde objektive Anhaltspunkte der Coronararterienarflrankung bei Patienten unter 50 Jahren, die kiene Abnormalität bieten, weder bei der physikalischen Untersuchung, noch bei der Herzdurchleuchtung, der Thorax-Röntgenaufnahmen dem EKG mit 12 Ableitungen in Ruhe und "Stress-Testen."

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Cyanacethydrazide Therapy in Pulmonary Tuberculosis

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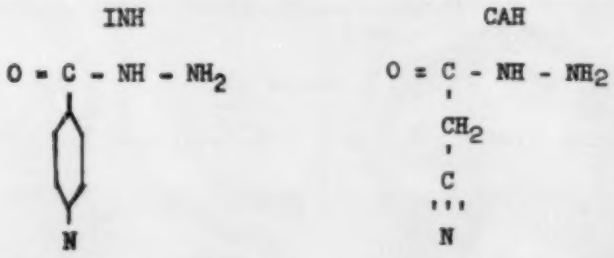
The efficacy of isoniazid in the treatment of pulmonary tuberculosis stimulated the search for related drugs that might increase the effectiveness of antituberculosis therapy especially in those chronically ill patients in whom INH does not produce the desired effect or who are unable to tolerate it. Such a compound is cyanacethydrazide** which as its formula indicates is structurally related to INH.



The introduction of this drug was based on the reasoning[1] that the specific arrangement of the nitrogen atoms in the pyridine nucleus and the side chain, and not the pyridine nucleus as such were responsible for the action of INH and therefore the substitution of an aliphatic chain for the pyridine nucleus would allow for less toxicity while retaining its chemotherapeutic effectiveness. It was also felt by these investigators that this substitution would be less likely to produce bacillary resistance. CAH like INH had been synthesized about a half century earlier without attempt having been made to find therapeutic application for it.

Promising results with this drug were reported by European investigators[2-5] in limited studies. CAH has been studied at Eagleville for the past two years. The object of the study was to determine:

1. The toxicity of the drug and its acceptability by patients.
2. The presence of cross resistance to INH.
3. The clinical effectiveness of the drug.

The study comprised 150 patients who were treated with CAH for varying periods. Our clinical results are based on an analysis of 75 who used the drug from four months to one year or longer. The other 75 left the sanatorium or discontinued treatment before they had used the drug

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Presented at Annual Meeting American College of Chest Physicians, Chicago, Ill., June 9, 1956
**Kindly supplied for this study by Lakeside Laboratories, Inc., Milwaukee, Wisconsin

four months. These patients are included in our observations on toxicity and bacillary resistance.

CAH was used primarily on those with far advanced pulmonary tuberculosis who were still sputum positive on smear and culture in spite of long term antimicrobial (INH) therapy. Thirteen whose organisms were INH resistant were given the drug. There were three who were unable to tolerate INH. Twenty new admissions with active disease who had had no previous INH therapy were included in the study. The ages of the patients ranged from 20 to 70 years. The study comprised all types of pulmonary tuberculosis except miliary disease.

The dose of the drug varied from 5 to 15 milligrams per kilogram of body weight. It was given in 50 mg. tablets. The average dose ranged from 450-600 mg./day in three divided doses. Since the drug was studied as a substitute for INH, it was used like INH in combination with streptomycin and/or para-aminosalicylic acid. Pneumoperitoneum and surgery were not withheld when indicated.

Results

A—Toxicity:

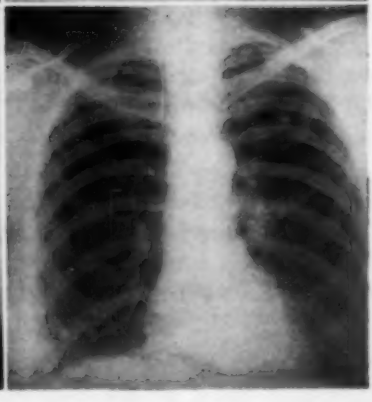
The drug was well tolerated even in the large doses used. There was

FIG. 1A

FIG. 1B

FIG. 2A

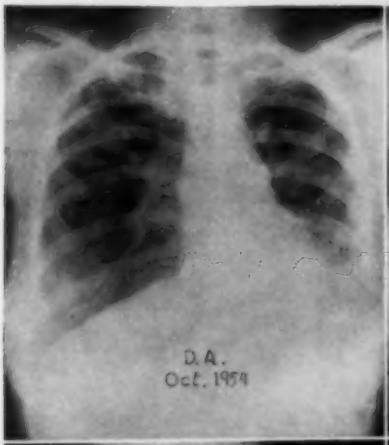
FIG. 2B



Case Nos. 7962 and 7914.

no toxic effect evident clinically or by laboratory studies. The patients followed the normal sanatorium regimen and were closely observed clinically by the resident physicians, nurses, and attending physicians. There was no instance of drug fever, tachycardia, arrhythmia or changes in blood pressure. There were no noticeable or ascertainable effects on bowel or urinary bladder function. Vertigo occurred after a few doses in a 66 year old white man with chronic auricular fibrillation and was severe enough for him to discontinue the use of the drug. He was able to tolerate INH without difficulty. Numbness and tingling of the hands and feet occurred in one but was mild and with B6 the patient continued the drug. The commonest complaint was headache, which although not severe occurred in approximately 10 per cent of the patients. This was usually related to large doses of the drug, 500-600 mg./day. The headache would

FIG. 3A



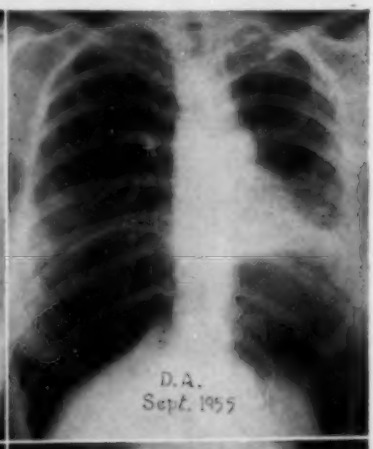


FIG. 3B

FIG. 4A

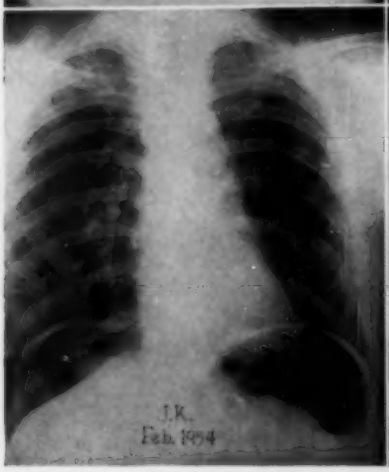


FIG. 4B

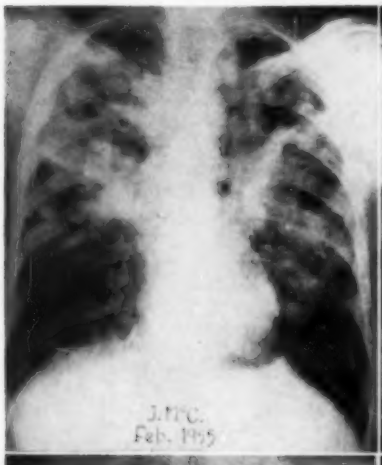
Case Nos. 7997 and 7766.

disappear if the dose was reduced slightly, or if the drug was begun in low dosage and gradually increased. In those who persisted with the drug without reducing the dose, the headache gradually subsided. There was no instance of jaundice or hematopoietic change. The laboratory studies included complete blood count, urinalysis, fasting blood sugar and urea nitrogen. Liver function studies included blood proteins with A/G ratio, cephalin cholesterol and thymol turbidity. These studies were repeated routinely during the drug investigation. A noticeable effect and one which was frequently commented on, especially by the younger women, was the infrequency of acne as compared to INH.

B—Resistance and Cross Resistance Studies:

All admissions to the sanatorium have routine sputum studies both by

FIG. 5A



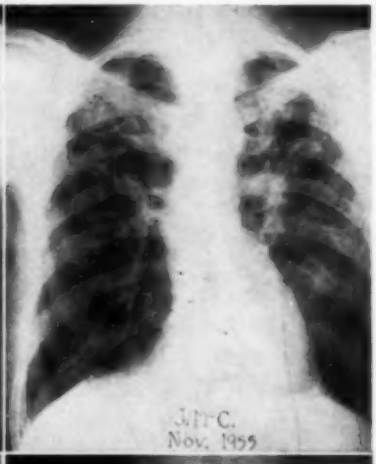
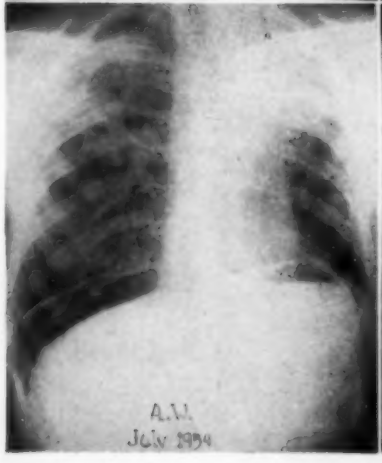


FIG. 5B

FIG. 6A



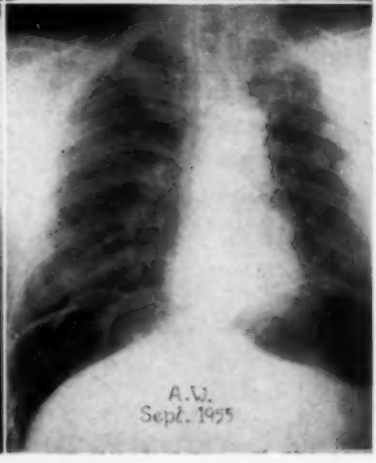


FIG. 6B

Case Nos. 8095 and 7954.

smear and culture. The organisms are tested for susceptibility to streptomycin, and isoniazid according to the technique outlined in the 1955 revision of Tuberculosis Laboratory Methods.[6] The same technique was followed with CAH, and organisms were routinely tested with 50 micrograms of CAH inoculated into the culture medium. 400 patients form the basis of this study. Sputum studies were done routinely as is the custom at Eagleville. Susceptibility studies were repeated usually at three or at the most, six month intervals.

1. *Resistance to INH:*

Twenty-one patients were found resistant to INH. These all had chronic disease and long term INH therapy. There was no patient naturally resistant to INH (without previous INH therapy).

Thirteen were INH resistant prior to treatment with CAH.

Eight showed resistance after treatment with CAH for periods of three months to one year.

Six of them had had long term treatment with INH prior to use of CAH.

Two who became resistant had used INH only for a few weeks prior to CAH therapy. These were the only definite instances of cross resistance. In both cultures six months later revealed organisms susceptible to both drugs.

Three who developed INH resistance remained susceptible to CAH and could continue with the drug.

2. *Resistance to CAH:*

Resistance to CAH was encountered in 34 patients.

Seven were found to be naturally resistant. They were new admissions who had had no previous antimicrobial drugs. The initial sputum culture showed organisms resistant to CAH. This is difficult to explain but is too large a group to ascribe to technical error.

Twenty-seven were found to harbor resistant organisms after treatment with CAH. The time interval varied from three months to over a year.

Three developed resistance rapidly, after days to a few weeks. They had had long term treatment with INH previously.

3. *Streptomycin Resistance:*

Twenty-nine were found resistant to streptomycin. They had chronic disease and long term antimicrobial drug treatment. There was no instance of natural resistance to streptomycin. There was no evidence of definite relationship between streptomycin resistance and CAH resistance as there appeared to be between INH and CAH resistance. Those with advanced chronic cavitary disease who developed resistance to streptomycin/INH usually showed resistance to CAH at some time during the course of the study.

4. *Changing Susceptibility Patterns:*

Five who exhibited streptomycin resistance later showed susceptibility.

Seven who were both INH and CAH resistant showed susceptibility to both drugs in later cultures.

These changing resistance patterns apparently reflect the mixed bacterial population that chronically ill persons harbor. One, a 40 year old man, with bilateral upper lobe disease with a cavity in the left upper lobe showed CAH resistant organisms on culture. Following resection of the left lobe, sputum cultures revealed organisms susceptible to CAH.

New admissions who had had no previous antimicrobial drug treatment, and who did not show sputum conversion after six to nine months of CAH were routinely changed to INH. As indicated above there were only two instances of apparent cross resistance to INH and these patients showed susceptible organisms on later cultures.

These resistance studies appear to bear out the *in vitro* investigations of Barclay[7] who found that organisms resistant to CAH remained susceptible to INH and that INH resistant organisms were partially sensitive to CAH in large doses.

C—Clinical Effectiveness:

The therapeutic effect of CAH is of the order of INH although much less so. It must be remembered that the great majority of the patients had chronic disease with prolonged INH administration previously. In general, the effect on fever, toxicity, cough and sputum was similar to INH, although certainly less dramatic. As with INH, appetite was stimulated and weight gain was common. The patients were given CAH as a routine therapeutic measure without preliminary discussion in order to minimize psychological bias.

One hundred and fifty were treated with CAH.

Seventy-five for four months or longer and form the basis for our clinical results.

Twenty-eight converted to negative sputum smear and culture and were discharged.

Two relapsed and were readmitted for surgery.

Four who converted had surgery.

Eleven were new admissions, in general, with new disease and had had no previous drug treatment. Their improvement was noted by x-ray films clearing as well.

Seventeen had had drugs previously over long terms. They responded more slowly but converted and remained negative. The x-ray film changes were not too marked although cavity closure and clearing was seen.

There was no patient INH resistant who turned negative with CAH, although seven who showed favorable clinical response left the sanatorium before they had taken the drug more than three months.

X-ray film changes were not significant except in those with acute or subacute (exudative) disease. The drug appeared more effective in larger dosage. Attempts to correlate blood levels of the drug with clinical effectiveness were unsuccessful. It was our feeling that the laboratory method was unreliable and the figures were, therefore, not included in this study.

CASE REPORTS

Case No. 7962, M. B. (Figure 1A, 1B): This white 60 year old diabetic housewife was admitted July 10, 1954 with chronic fibroid tuberculosis and essential hypertension. She had been followed by x-ray film inspections for many years and was always sputum negative. No treatment had been administered. On admission she had positive sputum, fever with bilateral cavitary apical disease. Diabetes was controlled by diet and 15 units of NPH insulin. CAH 600 mg. daily and streptomycin one gram twice weekly were administered. Her sputum was negative on September 23, 1954. She was discharged November 2, 1954 with negative sputum both by smear and culture and has remained so. No great change occurred in x-ray film appearance. She gained 23 pounds.

Case No. 7914, E. H. (Figure 2A, 2B): This white 48 year old waitress was admitted April 28, 1954 following discovery of a left upper lobe exudative lesion in routine annual food handler survey. Her sputum was positive. Drug treatment consisted of streptomycin one gram twice weekly. CAH was started 200 mg./day and gradually increased to 600 mg./day. Her sputum converted in September 1954 and she was discharged October 30, 1954 and has remained negative with satisfactory x-ray film clearing. Her weight gain was 13 pounds.

Case No. 7997, D. A. (Figure 3A, 3B): This white 23 year old housewife was admitted September 29, 1954 with history of tuberculosis dating to 1946. She had previously been institutionalized and received streptomycin, PAS and bilateral pneumothorax from 1946 to 1952. Following discharge she remained well and was followed in chest clinic. After the birth of baby in June 1954 she developed toxic symptoms and x-ray film showed evidence of progression. Her sputum was positive. She was treated with streptomycin one gram twice weekly, PAS 12 grams daily, CAH 450 mg./day and artificial pneumoperitoneum. She responded well and has had negative sputum since November 30, 1954. She was discharged on February 23, 1955 and has remained well.

Case No. 7766, J. K. (Figure 4A, 4B): This white obese printer 30 years of age was admitted with history of onset March 4, 1953. He had extensive disease and positive sputum. He received streptomycin, PAS and INH. Drugs were continued at Eagleville and pneumoperitoneum induced October 28, 1953. He remained positive and on April 21, 1954 PAS and INH were discontinued. He was then given CAH and PAS. He received 750 mg. CAH/day and converted on October 14, 1954. There was satisfactory clearing of lung fields on x-ray film and sputum has remained negative.

Case No. 8095, J. McC. (Figure 5A, 5B): This white 41 year old truck driver was admitted February 19, 1955 with history of acute onset. He was markedly underweight, toxic, had far advanced bilateral exudative disease and positive sputum. Streptomycin one gram daily and later one gram twice weekly, PAS 12 grams daily and CAH 600 mg./day were administered. He showed excellent clinical response and his sputum converted on August 25, 1955. He was discharged at his request December 10, 1955 with a weight gain of 34 pounds.

Case No. 7954, A. W. (Figure 6A, 6B): This male Negro of 32 years was admitted July 7, 1954 with positive sputum. Streptomycin one gram twice weekly, PAS 12 grams daily and CAH 450 mg./day were prescribed. His sputum converted by May 24, 1955 and remained so. He was discharged on September 16, 1955 with a total gain of 32 pounds.

Discussion

CAH has had extensive clinical trial at Eagleville Sanatorium. Clinical improvement and weight gain were common findings, but may be discounted because of use of other drugs and excellent sanatorium care. However, because of absence of toxicity and frequency of sputum conversion (35 per cent) it is evident that the drug has merit.

It has produced results in chronic retreatment cases as well as in new ones without evidence of toxicity. The problem of cross resistance must be considered since two patients who had had only a few weeks of INH were found to be INH resistant after CAH therapy, and six long term INH patients who were INH susceptible showed INH resistance after receiving CAH.

SUMMARY

1. Cyanacethydrazide appears to be an effective antituberculosis agent although less so than isoniazid.

2. It is non-toxic and is well tolerated in large doses.
3. Resistance studies indicate that it may possibly impair the usefulness of isoniazid.
4. It appears to be of limited value in isoniazid resistant patients.
5. It is a valuable drug for those who cannot tolerate INH.

The writer wishes to acknowledge his indebtedness to Miss Betty Kane, bacteriologist, and to the Staff of Eagleville Sanatorium for their assistance in this study.

RESUMEN

1. La Hidracida cianacética parece ser un medicamento antituberculoso efectivo aunque menos que la isoniacida.
2. No es tóxico y es tolerado en grandes dosis.
3. Los estudios sobre resistencia indican que quizá puede ser desfavorable para la utilización de la isoniacida.
4. Parece que es de poca utilidad en los enfermos con isoniacida resistencia.
5. Es una droga valiosa para los que no toleran la isoniacida.

RESUME

1. L'hydrazide cyanacétique semble être une médication antituberculeuse efficace, bien qu'à un degré moindre que l'isoniazide.
2. Il n'est pas toxique et est bien toléré à hautes doses.
3. Des études sur la résistance montrent qu'il est peut-être possible que ce produit gêne l'utilisation de l'isoniazide.
4. Son action semble limitée chez les malades résistants à l'isoniazide.
5. C'est une médication valable pour ceux qui ne supportent pas l'isoniazide.

ZUSAMMENFASSUNG

1. Cyanacethydrazit scheint ein wirksamer antituberkulöser Stoff zu sein, wenngleich in geringerem Grade als INH.
2. Er ist nicht toxisch und wird in hohen Dosen gut vertragen.
3. Resistenzbestimmungen ergeben, dass er möglicherweise die Brauchbarkeit von INH beeinträchtigen kann.
4. Er scheint von begrenztem Wert bei gegen INH resistenten Patienten.
5. Er ist ein wertvollen Medikament für solche Fälle, die INH nicht vertragen können.

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Mediastinal Emphysema and Left Pneumothorax

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Some patients were recently encountered presenting with Hamman's sign—crunching noises heard on auscultation over the precordium. This sound has been considered to indicate the presence of air in the mediastinum, but while mediastinal emphysema was found in some of the patients others had a shallow left-sided pneumothorax only. Details of these cases are given here together with certain conclusions drawn after examining the recorded cases of spontaneous mediastinal emphysema.

Air may enter the mediastinum in a number of ways. It can travel down the fascial planes in the neck following wounds and operations such as thyroidectomy or tracheotomy, or it may escape from perforations of the trachea, bronchi, or esophagus. It can ascend from the retroperitoneal space, as in presacral pneumography and diagnostic pneumomediastinum[1] (Fig. 1), and has sometimes been reported as a complication of pneumoperitoneum. In this last event the route taken by the air, apart from accidental introduction outside the peritoneum or extraperitoneal escape at the site of puncture, is uncertain: there are a number of theoretical possibilities of which peritoneal rupture through the esophageal hiatus is the most likely.[2] Mediastinal emphysema has occasionally followed perforation of peptic ulcer.[3] Injury to the chest, with or without rib fracture, blast, chest operations, and induction of artificial pneumothorax when the needle penetrates the interstitial tissues of the lung, can all cause emphysema in the mediastinum.

Of special interest, however, is mediastinal emphysema following nontraumatic pulmonary interstitial emphysema. This last entity was clearly described by Laennec[4] who called it "interlobular emphysema," and he recognized that violent exertion, prolonged breath-holding and bronchial obstruction were causes. He also hinted at its spontaneous occurrence. Pulmonary interstitial emphysema occurred in some of the cases of influenzal pneumonia of Torrey and Grosh[5] and Berkley and Coffen.[6] Many instances of mediastinal emphysema have been recorded during exertion, straining with the glottis closed—especially in the second stage of labor (Figs. 2, 3, 4, 5)—anesthesia, bronchial asthma, infections such as tuberculosis, pneumonia and measles, atelectasis of the newborn, and in association with foreign bodies in the bronchus. It was Hamman[7, 8, 9, 10] who first emphasized the spontaneous occurrence of mediastinal emphysema and a number of cases have been reported since. The term "spontaneous" is perhaps open to some criticism as in many patients there were predisposing causes such as a mild respiratory infection or exercise, while in others similar factors may have been unnoticed.

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The mechanism of interstitial emphysema of the lungs and mediastinum is indicated by the experiments of Macklin.[11, 12] Catheters were passed into the bronchi of cats, and air blown in under pressure was shown to have ruptured from the alveoli into the interstitial tissue of the lung, dissecting its way along the sheaths of the pulmonary vessels to the root of the lung and mediastinum. From here it passed into the fascia and subcutaneous tissues of the neck (whence it could become distributed over the whole body), into the retroperitoneal tissues, and, by rupturing through the thin mediastinal pleura, into the pleural cavities producing bilateral pneumothorax. Neither in these experiments nor those of Griffin,[13] in which similar results were obtained by putting tracheotomized dogs into a decompression chamber, did the air rupturing from the mediastinum have a predilection for either the left or right pleural cavity. Thus a sequence of events was demonstrated, starting with alveolar rupture and pulmonary interstitial emphysema, leading to mediastinal emphysema, and finally subcutaneous emphysema and pneumothorax. Macklin went so far as to suggest that this was the usual mechanism for the production of spontaneous pneumothorax, despite the fact that in the large majority of

FIGURE 1: Chest radiograph of a case in which presacral pneumography had been carried out for a suspected adrenal tumor. A layer of air is seen along the left cardiac border, and there are streaks of air in the superior mediastinum and neck.

cases of this condition there is no evidence of mediastinal emphysema. He emphasized the role of atelectasis in producing local over-inflation and subsequent rupture of neighboring alveoli. The usual way a pneumothorax is produced, however, is by rupture of an alveolus or bulla directly through the visceral pleura, and it is conceivably possible that air might subsequently pass through the mediastinal pleura from the pleural cavity into the mediastinum.

The principal symptom of mediastinal emphysema is sudden pain, usually substernal with radiation to the neck, back, left shoulder and arm. It is variable in intensity, tending to be worse on inspiration, on movement, especially of the neck, when lying down, and when swallowing. It may sometimes closely simulate the pain of myocardial infarction, pulmonary embolus, dissecting aneurysm or pericarditis. The spontaneous variety is nearly always benign and there is little in the way of constitutional symptoms, but sometimes, especially when secondary to another condition such as chest injury, there is severe dyspnea (associated with "splinting" of the lungs by interstitial air), cyanosis, venous stasis and shock, and several deaths have been recorded. In their influenzal cases, Torrey and Grosh made the interesting observation that a few patients, when in extremis, developed sudden substernal pain and subcutaneous crepitation in the root of the neck, with marked relief from their dyspnea and cyanosis, indicating that the interstitial emphysema in the lungs was relieved by the sudden escape of air into the mediastinum and neck.

Laennec considered that there was one auscultatory sound completely pathognomonic of the condition, namely the dry crepitous rhonchus with

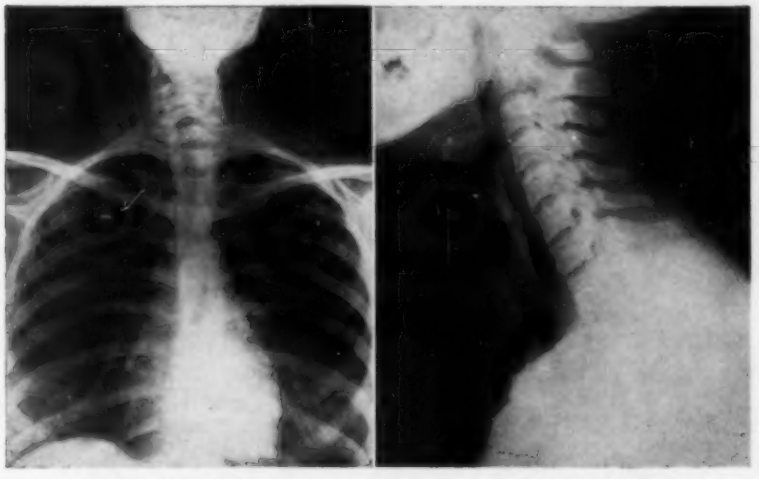

FIGURE 2 FIGURE 3

Figures 2 and 3: Posteroanterior and lateral radiographs of neck in a case of mediastinal emphysema occurring during labor. There is a zone of translucency along the right cardiac border, and air in the neck is clearly seen.

large bubbles ("le râle crépitant sec à grosses bulles"). It was almost certainly the same sign which was rediscovered by Hamman and which usually bears his name—crackling, bubbling, crunching sounds synchronous with the heart beat, inconstant, varying with position, and often loud enough to be heard by the patient. Hamman wrote of the first case he saw:

"... the patient laughingly said he could reproduce the sound. He turned on his left side, shifted about a few moments and suddenly said, "There it is." I put my stethoscope over the apex beat of the heart, and with each impulse heard the most amazing sound. It is difficult to describe. Crunching is the best adjective I can think of though it is far from apt especially since crunching has been widely used to describe pleural friction to which it bore no resemblance. It certainly conveyed the impression of air being churned or squeezed about in the tissues. . . . . When the patient turned on his back the sound at once disappeared."

X-ray film in this instance was normal and Hamman was unable to make a diagnosis until he encountered the same noise in another patient who had subcutaneous emphysema and radiologic evidence of air in the mediastinum. He then came to regard the sign as diagnostic of mediastinal emphysema, and this opinion has been unquestioningly accepted by nearly

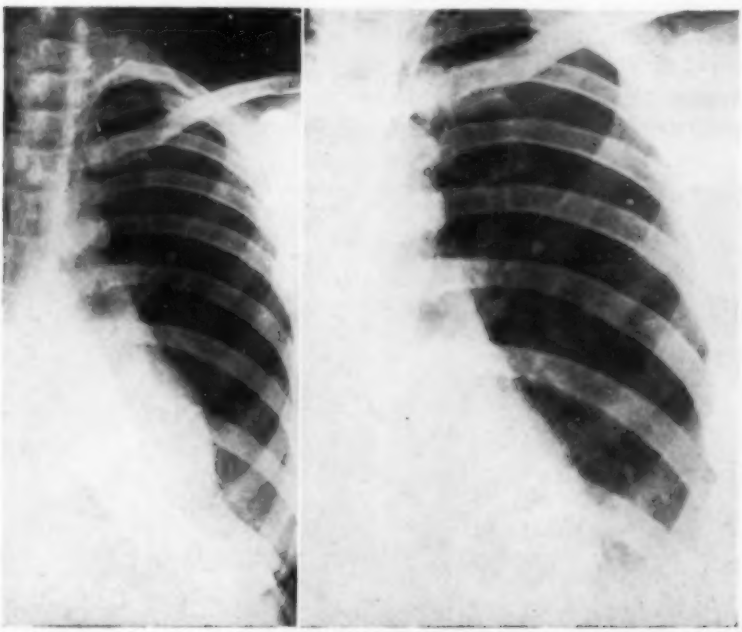

FIGURE 4 FIGURE 5

Figures 4 and 5: Chest radiograph in a case of mediastinal emphysema occurring during labor. There are streaks of air in the neck and superior mediastinum and a thin line is seen running parallel with the left border of the heart, probably representing parietal pleura lifted from the pericardium by air.

all subsequent authors. Other signs mentioned by Hamman are obliteration of cardiac dullness (which also occurs in vesicular emphysema and left pneumothorax); subcutaneous emphysema; and coexisting pneumothorax.

Left-sided pneumothorax itself, however, is known sometimes to produce a sound synchronous with the heart beat. Rees and Hughes[14] described a tapping sound in left-sided chest wounds probably due to pneumothorax, and Smith[15] recorded the same phenomenon, using the term "pericardial knock." Scadding and Wood[16] found clicking sounds in four cases of left-sided spontaneous pneumothorax and two of left artificial pneumothorax, due, they thought, to separation of the pleurae during systole. They also listened to a case of pneumomediastinum following presacral pneumography and thought that the sound they heard differed in quality from that of pneumothorax; a view shared by Greene.[17] Chapman,[18] on the other hand, heard crunching crackling noises at the cardiac apex in ten cases, in each of which there was a left spontaneous pneumothorax, and so considered that the sign was by no means pathognomonic of mediastinal emphysema.

Ninety-eight recorded cases of spontaneous mediastinal emphysema have been examined.[7-10, 17, 19-63] In some of the reported cases it is difficult to determine to what extent exertion was a factor, and it was therefore decided not to exclude cases occurring during exercise, even if this was occasionally considerable.[37,58] Usually, however, a history of antecedent exertion was not obtained. In some instances a concurrent mild respiratory infection was

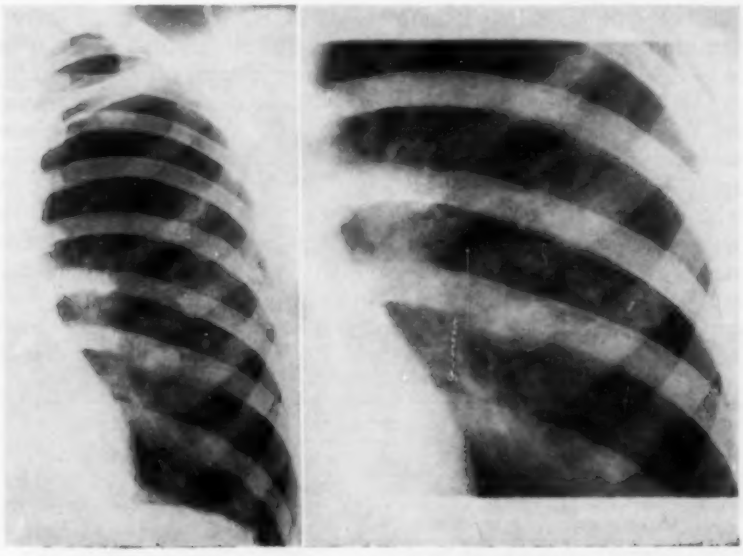

FIGURE 6 FIGURE 7

Figures 6 and 7: Chest radiograph of left artificial pneumothorax in a case of pulmonary tuberculosis. There was no evidence in this case to suggest the presence of mediastinal emphysema, but the thin line running parallel with the left cardiac border is similar to that seen in Figure 5.

noted. Not included in this series, however, were cases of mediastinal emphysema happening during labor, in the newborn, or obviously secondary to gross pulmonary conditions such as pneumonia or bronchial asthma.

An examination of the series reveals some interesting points (See Table). In all except eight cases the diagnosis of mediastinal emphysema was based mainly or entirely on Hamman's sign—crackling sounds synchronous with the heart beat. In these eight cases it was sought but not found in seven, and in one it was not mentioned; but in all eight there was subcutaneous emphysema and radiological evidence of pneumomediastinum.

Of the 98 cases, left pneumothorax, usually quite small, was found in no fewer than 48. Right pneumothorax was found in four cases only, and in one there was bilateral pneumothorax.

Subcutaneous emphysema in the neck or chest (which can be regarded as good confirmatory evidence of mediastinal emphysema) occurred in 27 of the 98 cases. In these 27 cases left pneumothorax was present in only five, and right pneumothorax in one. In the remaining 21 there was no pneumothorax demonstrated.

In 18 of the 98 Hamman's sign was the only abnormal finding; there was no subcutaneous emphysema and chest radiograph was normal (or in one case not taken). The association of Hamman's sign and left pneumothorax, with no other suggestion of pneumomediastinum, occurred in 28; with right pneumothorax in three; and bilateral pneumothorax in one.

In 38 cases radiological evidence of pneumomediastinum was claimed, and in three "probable" or "possible"—41 in all. In 17 of these there was left pneumothorax. The x-ray film evidence for mediastinal emphysema in these 17 cases was in three merely the mention of "air in the mediastinum"; in four it consisted of "possible" air between the heart and sternum on lateral view (which we regard as uncertain evidence in the presence of pneumothorax); one had a doubtful bubble of air in the posterior mediastinum; and in nine there was a translucent zone along the left cardiac border. This last sign has been generally accepted as representing air in the mediastinum (between the pericardium and parietal pleura); but, as Chapman points out, a zone of lucency along the left cardiac border may be due to air trapped between the lung and heart (between the parietal and visceral pleura). The difficulty of interpreting a line parallel to the left border of the heart is illustrated in Figures 6 and 7, which show an x-ray film of an

Number of cases reported as mediastinal emphysema	98	
Hamman's sign present	90	
Left pneumothorax present		48
Right pneumothorax present		4
Bilateral pneumothorax present		1
Number of cases with subcutaneous emphysema	27	
Left pneumothorax present		5
Right pneumothorax present		1

established left-sided artificial pneumothorax in which there was no evidence to suggest mediastinal emphysema. The line parallel to the left side of the heart probably represents, in this case, the medial lung border. It is not dissimilar to that in Figures 4 and 5, from a case in which there was undoubtedly air in the mediastinum, as subcutaneous air was present in the neck. The bizarre appearance in Fig. 8 is from the same patient (with left artificial pneumothorax) as in Figures 6 and 7, radiographed when lying on the left side.

In cases where there was left pneumothorax, pain tended to be left-sided; but while in many cases without left pneumothorax pain was substernal only, in a greater number there was radiation to the left side of the chest, left shoulder and arm. The site and nature of the pain are therefore not of great help in determining the presence or absence of pneumothorax. Pain on swallowing is probably diagnostic of mediastinal emphysema, being present in four cases all of which had subcutaneous emphysema and none left pneumothorax.

Death occurred in three elderly patients[20, 51, 55] aged 78, 61, and 96. In each there was severe subcutaneous emphysema: one was complicated by myocardial infarction, and another by auricular fibrillation. The majority, however, were young adults, only 15 of the 98 being over the age of 35.

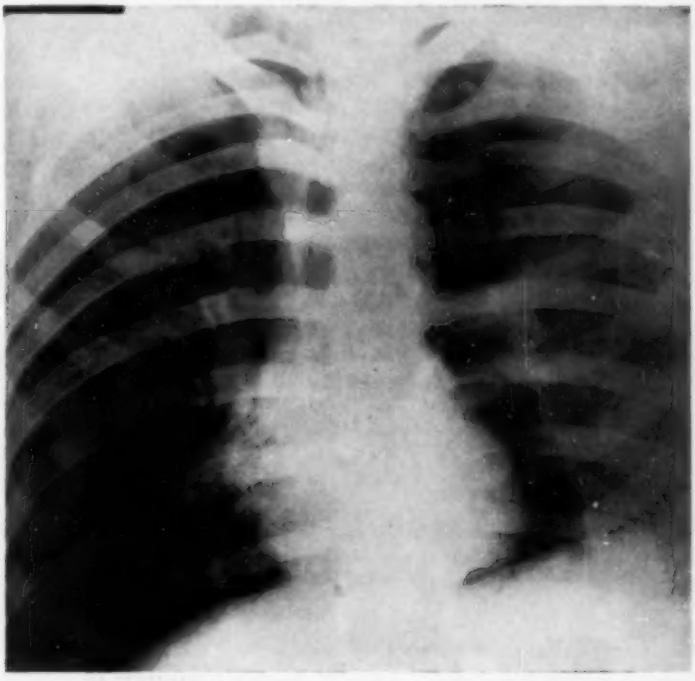

FIGURE 8: Chest radiograph of the same case as Figures 6 and 7, taken with the patient lying on the left side. There is a wide layer of air along the left border of the heart and mediastinum.

The course was usually benign although in six, incisions in the neck were needed to release subcutaneous air, a measure frequently performed for subcutaneous emphysema secondary to trauma and bronchial asthma.

The frequent occurrence of left pneumothorax in this series of cases might be explained by supposing that this condition often follows mediastinal emphysema. This has in fact been the usual explanation, although there is no anatomical reason for the left-sided preponderance, which as already mentioned has not been found in experimental work. Also striking is the much lower incidence of left pneumothorax in cases where the presence of mediastinal emphysema is confirmed by air in the subcutaneous tissues. It seems possible that many of the cases recorded as mediastinal emphysema may have been examples of uncomplicated left pneumothorax only, and that Hamman's sign may occur in both conditions. Such a hypothesis supposes that the sounds produced by the heart's action on bubbles of air in the mediastinum are indistinguishable from those produced when a small quantity of air between the layers of the pleura lies next to the heart. The hypothesis receives support from a study of the following seven personally observed cases, in all of which Hamman's sign was elicited. Though the sounds varied in intensity (and were of course heard at different times), no essential qualitative difference was observed from case to case. In two cases mediastinal emphysema, without pneumothorax, was certainly present, and in a third uncomplicated mediastinal emphysema was probable. In each of three other cases there was a small left pneumothorax, without mediastinal emphysema, while in the last case either condition may have been present, the radiological appearances being normal.

Case 1: Signalman A. S., aged 19. There was a history of asthma and pleurisy in childhood. He was admitted to the British Military Hospital, Fayid, Suez Canal Zone, on December 12, 1952, with a history of cough and purulent sputum of a day's duration. On the day of admission, while walking, he suddenly experienced severe

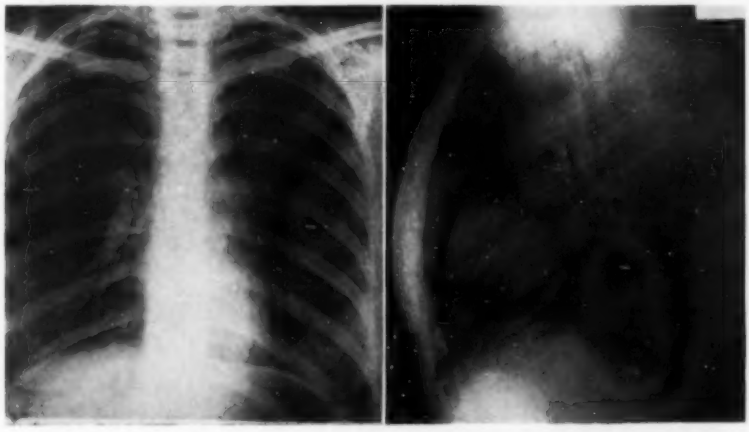

FIGURE 9 FIGURE 10

Figures 9 and 10: Chest posteroanterior and lateral radiographs in Case 2, showing streaks of air in the mediastinum.

continuous pain under the sternum, worse on inspiration. He was slightly short of breath.

On examination there was a slight fever. Subcutaneous emphysema was palpable in the left supraclavicular fossa. Chest movement was moderate and equal on both sides. The trachea was central. Vocal fremitus and resonance were equal on both sides. There was only slight cardiac dullness to percussion. Throughout the lungs a few scattered rhonchi were audible. Over the precordium were heard crunching crackling sounds synchronous with the heart beats: no variation with posture was noted. A posteroanterior radiograph was normal, there being no radiological evidence of pneumothorax.

He was treated with penicillin and ephedrine: in a few days he was symptom free and the abnormal signs had disappeared. Convalescence and return to duty were uneventful. In March 1956 he wrote that he had had no further trouble.

Case 2: Miss J. H., aged 21. Bank clerk. She had pneumonia in infancy and there was a three years' history of slight nocturnal wheezing occurring about once a month and also in foggy weather. Two days previously she had a head cold and on April 14, 1956 she was admitted to St. Mary's Hospital, London, having awakened early that morning with wheezing dyspnea, slightly eased by an injection of adrenalin but persisting during the day. In the afternoon she had slight pain behind the sternum, of abrupt onset, worse on inspiration, and which passed off after an hour or two.

On examination there was some dyspnea with expiratory wheezing. Her temperature was 100.0° F., pulse 120 and blood pressure 110/70. Subcutaneous emphysema was left in the right supraclavicular fossa, and later on the left side and in the suprasternal notch. The trachea was central. Chest movement was poor but symmetrical. Vocal fremitus and resonance were equal on both sides. Cardiac dullness to percussion was only just discernible. Throughout the lungs there were rhonchi with a few scattered rales. The second pulmonary sound was accentuated. Over the whole precordium there were showers of crunching noises, in systole and diastole, synchronous with the heart beat. They were easily heard on auscultation with the patient lying on her back, but

FIGURE 11

FIGURE 12

Figures 11 and 12: Chest posteroanterior radiograph in Case 3, showing the thin line running parallel with the left cardiac border.

were intensified when she turned on her left side.

Chest x-ray film showed streaks of air within the mediastinum on posteroanterior and lateral views (Figures 9 and 10). There was no pneumothorax. Electrocardiogram showed sinus tachycardia with prominent pointed P waves in leads 11 and 111 (P pulmonale); leads taken when standing showed clockwise rotation as compared with those taken lying down, but no other difference. From the sputum a mixed growth of proteus vulgaris and pneumococci was obtained.

Shortly after admission there was a brief recurrence of the chest pain, worse when lying on the left side and on inspiration. Following treatment with penicillin and antispasmodics she was soon free of symptoms. The subcutaneous air and crunching noises over the precordium disappeared in a few days. After her discharge on April 21 she remained well except for occasional slight morning wheezing. Subsequent chest x-ray film was normal and an electrocardiogram showed less prominent P waves than formerly with no change in heart position on standing.

Case 3: Mr. J. B., aged 44. Steel-erector. Since an attack of bronchitis in 1943 at the age of 32 he had chronic cough with a little yellow sputum in the morning. In 1950 he had right spontaneous pneumothorax, and pneumonia in 1953 and 1954. He also suffered with gastric and duodenal ulcers, confirmed radiologically.

He was admitted to St. Mary's Hospital on October 21, 1955. The previous evening, while sitting down, he had sudden sharp pain, worse on coughing and breathing, situated in the left scapular and interscapular regions. He was sweating, short of breath, and unable to sleep because of the pain.

On examination he was pale, sweating and slightly dyspneic. His temperature was 98.4° F., pulse 80 and blood pressure 120/70. There was no clubbing. No subcutaneous emphysema was palpable. The trachea was central. Chest movement was poor and slightly diminished on the left side. Cardiac and liver dullness to percussion were absent. Widespread rhonchi were audible throughout both lungs, and over the precordium there was a clicking crunching noise in systole, varying with respiration and more marked when lying on the left side.

Chest x-ray film showed slight inflammatory changes at the left base, and a single thin line running down parallel to the left border of the heart, with a similar line above the left dome of the diaphragm (Figures 11 and 12). A lateral film was not taken.

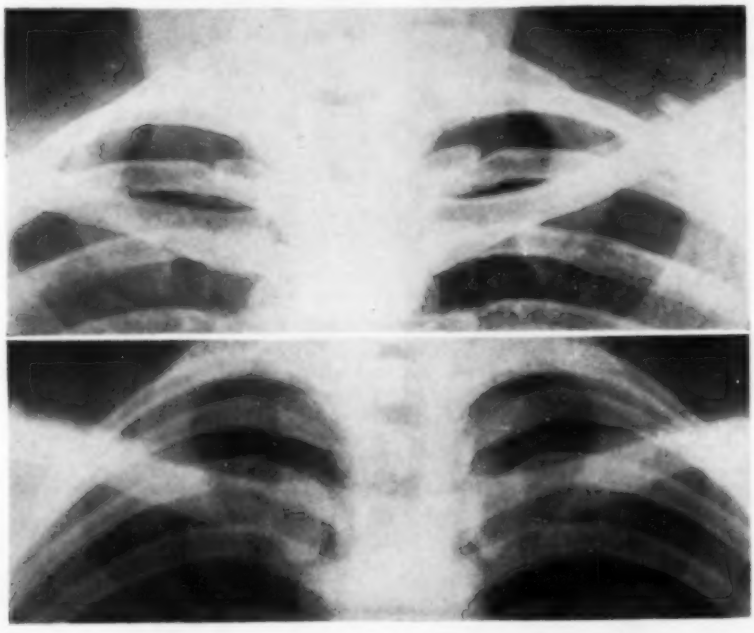

FIGURE 13: Part of chest radiograph in Case 4, showing small left pneumothorax.
FIGURE 14: Part of chest radiograph in Case 6, showing small left pneumothorax.

The pain and crunching sounds went in a few days, and the radiological abnormalities had gone by October 31.

In Cases 1 and 2 the diagnosis of mediastinal emphysema was confirmed by the presence of subcutaneous air in the neck, and in Case 2 by unequivocal x-ray film appearances as well. In Case 3 there was no subcutaneous air, and while the x-ray film suggests mediastinal emphysema it is possible that the lines are due to lung edge in the presence of pneumothorax, the layers of the costal pleura being adherent. In all three cases there was respiratory infection and bronchospasm.

Case 4: Mrs. M. G., aged 19. Housewife. She was quite well until the evening of February 25, 1956, when while walking she had a sudden sharp pain under the left breast radiating to the left shoulder. It persisted and was made worse by inspiration and lying on the left side. It woke her several times during the night. The next day the pain continued intermittently, and she noticed a crackling sound in the left side of the chest when she breathed deeply or lay on her left side. There was slight dyspnea initially but no other symptom. She was admitted the same day to St. Mary's Hospital.

On examination, her temperature was 99.4° F., pulse 100 and blood pressure 126/76. There was no subcutaneous emphysema. The trachea was slightly displaced to the right. Vocal fremitus was diminished over the left upper chest anteriorly. No difference in percussion note was observed on the two sides, but cardiac dullness was absent. Breath sounds were diminished over the left upper zone anteriorly. Crunching sounds, synchronous with the heart beat and occurring in systole and diastole, were heard over the sternum and left upper lobe: they were variable and intermittent, being best heard at the end of deep inspiration and lying on the left side.

Chest x-ray films (posteroanterior and lateral views) showed left apical pneumothorax with no mediastinal emphysema (Fig. 13). The electrocardiogram was normal. The red cell sedimentation rate was 2 mm. Mantoux 1/1000 negative. In three days the pain and abnormal signs disappeared, and x-ray film on March 3 was normal.

Case 5: Miss C. B., aged 18. Factory worker. On January 30, 1956, she felt a sudden pain in the left side of the chest while sitting quietly in the cinema: the pain lasted for a day or so. At that time she was seen in the Casualty Department, St. Mary's Hospital, where no abnormality was found except for slightly diminished breath sounds in the lower left axillary region. Chest x-ray film and red cell sedimentation rate were normal.

On April 3, 1956, she again came to the Casualty Department. She was now three months pregnant and had been attending the venereal disease clinic with vaginitis. On the previous day, while walking, she had a sudden severe pain in the left upper chest anteriorly, worse on inspiration and exertion, and during the night she awoke with a clicking sensation in the left side of the chest.

On examination, the temperature was 98.6° F., pulse 88 and blood pressure 120/80. There was no subcutaneous emphysema and the trachea was central. Chest movement and vocal fremitus were equal on both sides. Cardiac dullness to percussion was only just detectable. Breath sounds were normal. Over the precordium and upper sternum clicking and crunching noises synchronous with the heart beat were heard. They seemed to occur mainly in systole but were also heard in diastole, and they were accentuated when she lay on the left side.

Chest x-ray film showed a small left apical pneumothorax, with no evidence of air in the mediastinum. By the next day the pain had gone but there were still a few crunches to be heard especially when she lay on her left side. On her next attendance two days later (she was resting at home) physical examination and chest x-ray film were normal, and she remained well.

Case 6: Mr. R. B., aged 19. Forestry student. Admitted to Harefield Hospital, Middlesex, on March 22, 1956. He had been quite well until three days before when, while running up stairs, he had a sudden pain under the sternum radiating to the left shoulder. It lasted for a few minutes only, but recurred several times during the next few days, being sometimes accompanied by a clicking noise in the chest, more marked when he lay on his left side. There was no dyspnea and he was otherwise well.

On examination temperature, pulse, and blood-pressure were normal. There was no subcutaneous emphysema, the trachea was central, chest movement was normal and vocal fremitus was equal on both sides. There was a diminished area of cardiac dullness, the percussion note being otherwise normal. Breath sounds were normal, but over the precordium there were loud crackling crunching sounds in time with the heart beat, heard in systole and diastole. They were accentuated when he lay on his left side. Physical examination was otherwise normal.

Chest x-ray films (posteroanterior and lateral) showed small left apical pneumothorax with no evidence of mediastinal emphysema (Fig. 14). Electrocardiogram was normal.

The pain and abnormal sounds disappeared over the course of a few days and subsequent x-ray film was normal.

In Cases 4, 5 and 6 the sounds heard were similar to those in the first three, but all had small left pneumothorax with no emphysema of the mediastinum. In the next case the diagnosis remains uncertain as the same sounds were heard but x-ray film was normal and there was no subcutaneous emphysema.

Case 7: Miss M. W., aged 34. House Surgeon. She was admitted to St. Mary's Hospital on January 13, 1956. She was quite well until the afternoon of admission when, while she was standing examining a patient with an ophthalmoscope, there was the sudden onset of severe pain in the left chest anteriorly, radiating to the left shoulder, left scapular region, and down the left arm as far as the middle of the forearm. The pain was continuous but slightly worse on deep inspiration. The left hand felt weak and cold. She was considered by two doctors to have probably had coronary thrombosis, and had been given an injection of morphine.

By the time of admission the pain was less severe and there were no other symptoms, but she was extremely apprehensive as she herself thought that she had had coronary thrombosis. Her temperature was 98.4° F., pulse 80, respiration 20 and blood pressure 120/80. There was no subcutaneous emphysema, the trachea was central, and chest movements were equal. Vocal fremitus, percussion note and breath sounds were all normal, but on deep inspiration crackling sounds were heard over the upper sternum extending out over the left upper chest. They were not audible during quiet respiration. After a few deep breaths followed by breath-holding the sounds were also heard synchronous with the heart beats for a few beats only. Examination was other wise normal.

Chest x-ray films (posteroanterior and oblique views) were normal, with no evidence of mediastinal emphysema or pneumothorax. Electrocardiogram and red cell sedimentation rate were also normal. After two days she had no more pain and the unusual sounds in the chest had disappeared. She subsequently remained well.

In the last case a chest x-ray film was not taken in full expiration, and the possibility of shallow left pneumothorax is not excluded.

Griffin[29] states that crunching sounds are never heard in artificial pneumothorax. Recently, however, we did hear sounds similar to those in the cases above following induction of left artificial pneumothorax, and this was confirmed by other observers. The sounds came after about 100 cc. of air was introduced; as more air went into the pleural cavity they changed into a single systolic click, and then disappeared. There was no chest pain and no evidence to suggest mediastinal emphysema. It should be remembered that the sounds seem to occur with a small pneumothorax only, and are frequently heard with the patient lying on the left side—the opposite position to that assumed during induction of a left artificial pneumothorax.

It seems, then, that the sounds produced by shallow left pneumothorax and by mediastinal emphysema may be closely similar, and that the latter condition can be diagnosed with certainty only in the presence of subcutaneous air or the unequivocal radiological appearance of streaks of air in the mediastinum, a lateral x-ray film being usefu[1]. When Hamman's sign is encountered in the absence of these criteria a careful search should be made for left pneumothorax, and this should include a film taken during expiration.

SUMMARY

1. The results of examining 98 reported cases of spontaneous mediastinal emphysema are presented. In many of them the diagnosis was based

largely or entirely on the presence of Hamman's sign. In these 98 cases a small left pneumothorax was found in 48, but a right pneumothorax in only four.

2. Some personally observed cases are described in which Hamman's sign was elicited. Mediastinal emphysema was shown to be present in some of them, while others had only a small left pneumothorax.

3. It is suggested that many of the reported cases of spontaneous mediastinal emphysema may have had only uncomplicated small left pneumothorax, the auscultatory sounds produced by the two conditions being sometimes closely similar. In confirming the diagnosis of mediastinal emphysema, the importance is stressed of the presence of subcutaneous emphysema or definite radiological changes.

Permission to publish these cases and radiographs is due to the courtesy of Dr. W. D. W. Brooks, Dr. T. C. Hunt, Dr. E. Rohan Williams, and Dr. Basil Strickland, of St. Mary's Hospital, London; and to Dr. E. Idris Jones of Harefield Hospital, Middlesex.

RESUMEN

1. Se examinan los resultados del examen de 98 casos reportados de enfisema mediastínico espontáneo. En muchos de ellos el diagnóstico se basó grandemente en la presencia del signo de Hamman. En estos 98 casos un pequeño neumotórax izquierdo se encontró en 48, pero neumotórax derecho sólo en cuatro.

2. Algunos casos presonalmente observados se describen en los que el signo Hamman fué provocado. El enfisema mediastinal se demostró que estaba presente en algunos de ellos en tano que en otros sólo había un pequeño neumotórax izquierdo.

3. Se sugiere que muchos de los casos relatados de enfisema mediastinal espontáneo pueden haber sido sólo pequeños neumotórax izquierdos sin complicaciones ya que los signos auscultatorios producidos por los dos son a veces muy similares. Para confirmar el enfisema mediastínico se recalca que tiene importancia la presencia de enfisema subcutáneo o cambios radiológicos definidos.

RESUME

1. L'auteur présente les résultats d'un contrôle effectué sur 98 observations d'emphysème médiastinal spontané. Dans beaucoup de ces cas, le diagnostic fut basé entièrement ou pour une large part sur la présence du signe de Hamman. Sur ces 98 cas, on trouva un petit pneumothorax gauche chez 48 malades, mais chez 4 seulement un pneumothorax droit.

2. L'auteur décrit quelques cas qu'il a personnellement observés, où le signe d'Hamman faisait défaut. L'emphysème médiastinal existait chez certains d'entre eux, tandis que d'autres n'étaient poreurs que d'un petit pneumothorax gauche.

3. L'auteur suggère que beaucoup des cas considérés comme emphysème médiastinal spontané ne sont peut-être que de petits pneumothorax guaches sans complications, les signes d'auscultation dans les deux cas étant quelquefois très semblables. L'auteur met l'accent sur la nécissité d'emphysème sous-cutané et d'altérations radiologiques précises pour affirmer le diagnostic d'emphysème médiastinal.

ZUSAMMENFASSUNG

1. Es werden die Ergebnisse vorgelegt über eine Nachprüfung von 98 veröffentlichten Fällen von spontanem mediastinalem Emphysem. Bei vielen von ihnen basierte die Diagnose überwiegend oder ganz auf dem Vorliegen des Hamman'schen Zeichen. Unter diesen 98 Fällen wurde bei 48 ein kleiner linksseitiger Pneumothorax gefunden, ein rechtsseitiger jedoch nur in 4 Fällen.

2. Es werden einige persönlich beobachtete Fälle beschrieben, bei denen sich das Hamman'sche Zeichen nachweisen liess. Es zeigte sich, dass das mediastinale Emphysem in einigen dieser Fälle vorhanden war, während andere nur einen kleinen linksseitigen Pneumothorax hatten.

3. Es wird die Vermutung ausgesprochen, dass viele der in der Literatur wiedergegebenen Fälle von spontanem mediastinalen Emphysem nicht erkannte unkomplizierte kleine linksseitige Pneumothorazes gewesen sind, da die auskultatorischen Geräusche, wie sie durch beide Krankheitszustände hervorgerufen werden, mitunter recht ähnlich klingen. Um die Diagnose des mediastinalen Emphysems zu sicher, wird die Wichtigkeit des Bestehens eines subkutanen Emphysems oder eindeutiger röntgenologischer Veränderungen betont.

References will appear in reprints.

Delayed Cardiac Arrhythmias Following Non-Cardiac Thoracic Surgery

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The frequency of cardiac arrhythmias following non-cardiac thoracic surgery is not generally recognized. Little or no reference to this subject is found in standard textbooks of cardiology or surgery. In 1920, Levine[1] called attention to the occurrence of cardiac arrhythmias following general surgical procedures, such as cholecystectomy and herniorraphy, but no thoracic surgical procedure was mentioned. Since 1943, there have been several reports of post-thoracotomy arrhythmias,[2-7] with a total of 67 arrhythmias following 544 thoracotomies, an incidence of 12.3 per cent.

During a two year period at the Philadelphia Veterans Administration Hospital, 92 patients who underwent thoracotomy for non-cardiac disease were studied with respect to the incidence of cardiac arrhythmias, their type and time of onset, duration and response to treatment. The cases were also studied to see whether any correlation could be found between the occurrence of arrhythmias and the age of the patient, his preoperative cardiac status, and various factors in the postoperative period. Arrhythmias that occurred during operation were excluded from the series.

Results

Incidence: Of the 92 patients, 15 (16.3 per cent) developed postoperative arrhythmias. Several had two or more episodes with a total of 21 arrhythmias in the group.

Type of Surgical Procedure: (Table I) There were 16 who had pneumonectomies of whom 6 (37.5 per cent) developed arrhythmias. Of 24 who had thoracotomy and biopsy without a definitive surgical procedure, 8 (30 per cent) developed postoperative arrhythmias. Only one of 22 patients who had lobectomies and none of 20 who had segmental resections developed arrhythmias. There was no arrhythmia among a miscellaneous group of three exploratory thoracotomies, four decortications, one pleural stripping, and two drainages of empyema.

Type of Arrhythmia: (Table II) The 15 patients had a total of 21 episodes of arrhythmia. Seven had atrial fibrillation, four atrial flutter, two atrial tachycardia, and two multiple atrial premature contractions. There was no ventricular arrhythmia.

Time of Onset of Arrhythmia: In five cases, the arrhythmia occurred on the first or second postoperative day. In 10, the arrhythmia occurred between the third and 14th day. In a patient with recurrent atrial flutter,

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episodes occurred on the 28th, 36th, 82nd, 96th, and 127th day. One arrhythmia developed five months after operation in relation to recurrent empyema.

Duration of Arrhythmia: In 13 cases, the arrhythmia lasted from one hour to five days. In one, it lasted 11 days. The most persistent occurred in a patient who had atrial flutter which was converted to atrial fibrillation. The fibrillation lasted 14 days before it finally was converted to normal sinus rhythm.

Method of Treatment: In all except five cases, normal sinus rhythm was restored following rapid digitalization. In one case, death occurred too soon after the detection of the arrhythmia for treatment to be instituted. One episode of atrial flutter and one of fibrillation were successfully treated with quinidine after first being controlled with digitalis. Two episodes of paroxysmal atrial tachycardia responded to prostigmin and carotid sinus pressure.

Age and Sex of Patients: (Table III) All of the patients were men. The hospital population is, however, predominantly adult men. Among 32 patients under 50 years of age only one (3.1 per cent) arrhythmia occurred. This was in a 34 year old man who had extensive involvement of the heart by mediastinal lymphoma. He had had arrhythmias prior to surgery which were converted to normal sinus rhythm. Of 60 over the age of 50, 14 (23.3 per cent) developed arrhythmias.

Presence of Heart Disease Prior to Surgery: (Table IV) Of the 15 who developed arrhythmias postoperatively, 4 (26.6 per cent) had evidence of heart disease. Of the 77 who did not develop arrhythmias, 12 (15.6 per cent) had heart disease. Twelve with evidence of antecedent myo-

TABLE I

Type of Operation	Cases	Arrhythmias Number	Arrhythmias Per Cent
Pneumonectomy	16	6	37.5
Lobectomy	22	1	4.5
Segmental Resection	20	0	0.0
Exploration and Biopsy	24	8	30.0
Exploration—No Biopsy	3	0	0.0
Decortication	4	0	0.0
Pleural Stripping	1	0	0.0
Drainage of Empyema	2	0	0.0
TOTAL	92	15	16.3

TABLE II

Type of Arrhythmia	Cases	Arrhythmias
Atrial Fibrillation	7	8
Atrial Flutter	4	8
Atrial Tachycardia	2	3
Multiple Atrial Premature Contractions	2	2
Ventricular Tachycardia	0	0
TOTAL	15	21

cardial infarction, however, did not develop arrhythmias. Twenty per cent of the patients over age 50 had overt heart disease as contrasted with 12.5 per cent of those under 50. In none of the patients was there evidence of cardiac decompensation before operation.

Miscellaneous: No correlation was observed between the occurrence of cardiac arrhythmias and the presence of pulmonary infection prior to surgery, or with the presence postoperatively of fever, mediastinal shift, or hydrothorax. Arrhythmias were more frequent in patients who had mediastinal dissection, usually for neoplastic involvement of the mediastinal tissues. Autopsies have been performed on six who had arrhythmias, four of whom had metastatic tumor involving the epicardium and pericardium. Only two in the series had a postoperative course complicated by empyema and bronchopleural fistula. Both developed delayed cardiac arrhythmias.

Discussion

The development of cardiac arrhythmias during the manipulation of intrathoracic structures at the time of surgery is explained by much experimental evidence. Cabitt et al[8] produced a variety of arrhythmias in dogs while dividing the hilum of the lung and manipulating pulmonary vessels. Since the lungs had been collapsed early in the procedure, they inferred that the arrhythmias were caused by reflexes rather than by anoxia. Atrial and ventricular arrhythmias have been described following clamping of the main pulmonary artery[9] and during fatal pulmonary embolism.[10] Vagal stimulation has long been known to precipitate atrial fibrillation in animals, particularly under conditions of anoxia. Fibrillation has also been attributed to stretching of the auricle.[11] Cholinergic drugs have an additive effect with anoxia in favoring the development of arrhythmias.[12, 13]

From these observations it would seem that the arrhythmias associated with thoracic surgery would be most likely to occur during or immediately following the operative procedure. Manipulation of the pulmonary vessels and mediastinal dissection during surgery result in marked vagal stimulation, and there may be sudden stretching of the auricular musculature secondary to changes in pulmonary vascular pressure.

The explanation for the *delayed* onset of post-thoracotomy arrhythmias is more obscure. It is probable that anoxia plays a more important role at this time than it does during well controlled anesthesia. Jacoby and his associates[14] state that in hypoxic patients vagal stimulation from tracheal intubation caused a significant increase in the percentage of arrhythmias from 9 per cent in a well oxygenated group to 36 per cent in a hypoxic group. In the presence of chronic anoxia in the postoperative period, vagal stimulation may result from inflammatory reaction, neoplasm or infection. Bailey and Betts[2] reported that in 78 pneumonectomies, arrhythmias developed in eight, none of whom had evidence of heart disease prior to surgery. They noted that the vagus nerve which lies close to the bronchial stump, might be irritated by infection of the stump or by a silk suture. Massie and Vale[4] reported postoperative

arrhythmias in 9 per cent of 120 pneumonectomies. They could find no correlation between the arrhythmias and the type of lesion, its location, the presence of cardiac disease, manipulation of the vagus, or the occurrence of postoperative complications such as fever, mediastinal shift or empyema. Two cases, however, had extensive pericarditis at autopsy. The greatest incidence of arrhythmias in their series occurred in the 40-70 year age group. Humphreys[5] found a high incidence of arrhythmias (32 per cent) following pneumonectomy in an age group of 53-70 years, although the incidence following lobectomy was only 5 per cent. He considered vagal irritation and anoxia, in an age group where coronary insufficiency is frequent, to be the primary predisposing factors. Krosnick and Wasserman[7] studied 82 patients, all over age 50, with an incidence of arrhythmias of 12.2 per cent.

In our series it is apparent that the incidence of arrhythmias is much higher in the patients over the age of 50. Although there was no direct correlation with the presence of heart disease preoperatively, it may be assumed that those over 50 have a higher incidence of coronary sclerosis, and that this must play an important role in the development of arrhythmias. Other important factors appear to be the amount of mediastinal dissection, infection, and the presence of tumor tissue involving the heart and mediastinum.

SUMMARY

The frequency of delayed cardiac arrhythmias following non-cardiac thoracic surgery is greater than is generally recognized.

The average incidence in our series, consisting of 92 patients was 16.3 per cent. It was greatest after pneumonectomy (32.5 per cent) and

TABLE III

Age	Number of Patients	Arrhythmias Number	Arrhythmias Per Cent
Under 20	1	0	
21 - 30	11	0	
31 - 40	9	1	
41 - 50	11	0	
Under 50	32	1	3.1
51 - 60	33	7	
61 - 70	26	6	
71 - 80	1	1	
Over 50	60	14	23.3
TOTAL	92	15	16.3

TABLE IV

	Total	With Heart Disease Number	With Heart Disease Per Cent
With Arrhythmia	15	4	26.6
Without Arrhythmia	77	12	15.6
TOTAL	92	16	17.3
Under Age 50	32	4	12.5
Over Age 50	60	12	20.0
TOTAL	92	16	17.3

after mediastinal exploration and biopsy for neoplastic disease (30 per cent). The incidence was higher in those over 50 years of age.

All of the common atrial arrhythmias, including atrial fibrillation, atrial flutter, paroxysmal atrial tachycardia and multiple atrial premature contractions were observed. The majority of the arrhythmias occurred within two weeks postoperatively and responded to conventional therapy.

The probable cause of delayed cardiac arrhythmias is chronic vagal stimulation and anoxia in an age group where coronary sclerosis is prevalent. Infection or tumor implants in the pericardium and mediastinal tissues appear to be contributing factors in many cases.

RESUMEN

La frecuencia de las arritmias cardiacas retardadas después de cirugía de tórax no cardiaca, es mayor de lo que generalmente se admite.

El término medio de la incidencia en nuestra serie de 92 enfermos, fué de 16.3 por ciento. Fué mayor después de neumonectomía (32.5 por ciento) y después de exploraciones mediastinales y biopsia por neoplasias (30 por ciento).

La incidencia fué mayor en enfermos de más de 50 años.

Todas las arritmias atriales comunes, incluyendo la fibrilación atrial, flutter artial, taquicardia paroxística atrial, y las contracciones múltiples atriales prematuras, se han observado.

La mayoría de las arritmias ocurrieron dentro de dos semanas postoperatoriamente y respondieron a la terapia habitual.

La causa probable de las arritmias retardadas es la estimulación vagal crónica y la anoxia en el grupo de edad en que la esclerosis coronaria prevalece. La infección o las implantaciones tumorales en el pericardio y en los tejidos del mediastinoparecen ser factores contribuyentes en muchos casos.

RESUME

La fréquence des arythmies cardiaques tardives à la suite de la chirurgie thoracique pour affections non cardiaques est plus grande qu'on ne le reconnait généralement.

Le pourcentage moyen dans notre groupe comprenant 92 malades s'éleva à 16,3%. Il fut plus élevé après pneumonectomie (32,5%) et après exploration médiastinale et biopsie pour affection maligne (30%). La fréquence fut plus grande chez les malades âgés de plus de 50 ans.

Toutes les variétés d'arythmies banales, y compris la fibrillation auriculaire, la tachysystolie auriculaire, la tachycardie auriculaire paroxystique, et de multiples contractions prématurées de l'oreillette, furent observées. La majorité des arythmies survint dans un délai de deux semaines après l'opération, et fut jugulée par la thérapeutique banale.

La cause probable des arythmies cardiaques tardives est l'irritation chronique du pneumogastrique, et l'anoxie dans un groupe de malades âgés où la sclérose coronaire est prédominante. L'infection et les propagations tumorales du péricarde et des tissus médiastinaux semblent réaliser dans beaucoup de cas des facteurs prédisposants.

ZUSAMMENFASSUNG

Die Frequenz verzögerter cardialer Arrhythmien im Anschluss an nichtcardiale thoraxchirurgische Eingriffe ist grösser als allgemein angenommen wird.

Das durchschnittliche Vorkommen in unseren Gruppen, die aus 92 Patienten bestehen, betrug 16,3%. Es lag am höchsten nach Pneumonektomien (32,5%) und nach mediastinaler Untersuchung und Biopsie wegen Erkrankung an Neoplasmen (30%). Die Häufigkeit war grösser bei Personen über 50 Jahre.

Es wurden alle gewöhnlichen Vorhofs-Arrhythmien beobachtet, einschliesslich Vorhofflimmern, Vorhofflattern, paroxysmaler Vorhofs-Tachycardie und multipler vorzeitiger Vorhofskontraktionen. Die grössere Zahl der Arrhythmien trat innerhalb der ersten 2 postoperativen Wochen auf und sprach auf die übliche Behandlung an.

Die wahrscheinliche Ursache der verzögerten cardialen Arrhythmien ist ein chronischer Vagus-Reiz, und Anoxie in einer Altersgruppe, bei der die Coronarsklerose vorherrscht. Infektion oder in das Pericard und mediastinale Gewebe einwachsende Tumoren scheinen in vielen Fällen mitwirkende Faktoren zu sein.

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Should We Treat Tuberculin Converters?

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Should we or should we not treat primary tuberculosis? Answers to this question have gone from one extreme, that we should treat them all with preventorium care, to the other extreme, that none of them should be treated because those who had sanitorium care did no better than those who had none. Now that we have antituberculous drugs of relatively low toxicity, this same question has come up again. Whether or not we should treat primary tuberculosis depends upon the natural history of the disease; this history is determined by the age at which the patient has primary tuberculosis. The age group two years and under has a high incidence of serious complications, particularly tuberculous meningitis; the age group from five to nine years has very few complications from hematogenous spread of primary disease; the age group after puberty develops reinfection type pulmonary tuberculosis with the disease starting earlier in girls than in boys.

This question is asked most frequently by the pediatricians and I feel that we owe them an answer because out of 330 consecutive admissions to the Central Washington Tuberculosis hospital with proven tuberculosis (proved by positive culture or pathology), only 7 per cent were under six years of age, yet 56 per cent of the tuberculosis deaths occurred in this group.

Most physicians think of primary tuberculosis as a localized disease manifest by a Ghon complex and this is definitely not so because there is almost certainly hematogenous dissemination in all cases as manifest by:

1. The presence of small calcified tubercles in the spleen, calcified lymph nodes in the neck and abdomen, as seen on x-ray film or at autopsy;
2. The late complications of bone, renal and cervical adenitis;
3. Positive cultures of bone marrow as well as positive gastric washings in over 20 per cent of the patients, and
4. The fact that BCG organisms grown in radioactive phosphorous become radioactive, and when a person with a negative tuberculin is vaccinated with these radioactive organisms, it is possible to demonstrate radioactivity throughout the body within a few hours. If this occurs with an attenuated bacteria in the skin, then certainly it must occur with a virulent organism in the lung.

The object of giving antituberculous drugs is to sterilize the lesions already present. But there is no drug known today that will do this in an animal, even if the drug is started at the time the animal is infected; the combination of drugs that will sterilize the lesions in an animal is not a combination that anyone would even consider using in the treatment of

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primary tuberculosis since pyrazinamide has significant, serious toxic reactions. By the time the skin test has converted, the person already has caseous foci within the body, and streptomycin penetrates caseous material poorly; isoniazid is not effective in an area with low oxygen concentration such as these caseous areas. Unless tubercle bacilli are actively multiplying, none of these antituberculous drugs have any effect on them. The fact that some children have had a conversion of skin test from positive back to negative while taking isoniazid is no indication that all the tubercle bacilli are dead; this phenomenon was described by Dahlstrom in 1940 when he reported that 11 per cent of the children he followed became negative.

Dr. Edith Lincoln reported a year or so ago that she had never seen a child receiving isoniazid who developed tuberculous meningitis. Recently she reported a case, and there are at least four similar reports in European literature.

It was also reported that isoniazid resistant tubercle bacilli are not pathogenic to guinea pigs, yet if these same guinea pigs are kept for 90 days to nine months, some die of fulmuinating generalized tuberculosis and a significant number of them will have serious disease by the end of this time. We are not treating guinea pigs but people. Anyone who has had much experience with tuberculosis has seen patients die from progressive disease with izoniazid resistant organisms. Therefore, isoniazid resistant organisms are a serious complication, one on which the patient's life may depend. Among new admissions to the hospital, previously untreated, we are finding over 10 per cent with isoniazid resistant organisms.

The theoretical immunological value of a positive skin test is also very questionable because of those who acquired a primary infection from exposure, when followed for a long period of time (five to 20 years), a significant number developed reinfection type tuberculosis.

We have covered what antituberculous drugs will not do in the treatment of primary tuberculosis. What beneficial effects do they have? First, in my exprience in treating well over 100 children since 1952 using streptomycin, isoniazid and para-aminosalicylic acid, I have seen no new tuberculous complications after starting them on drug therapy. For example, no child admitted with miliary tuberculosis and normal spinal fluid has developed meningitis; no child with bone tuberculosis has developed meningitis even though fused early in the course of the disease. Our children have received an average of 220 days of combined drug therapy. The only ones who have received a year of drug therapy are those with tuberculous meningitis. Thus the complications that occur as a result of hematogenous spread of primary tuberculosis can be prevented with a much shorter period of treatment than is recommended by Lincoln. Combined drug therapy prevents new complications from hematogeneous spread. Since reinfection type tuberculosis occurs after puberty, and several years of follow-up are needed from the time of conversion of skin test to the breakdown with reinfection type disease, no one has a group of cases

large enough to give us information about the effectiveness of antituberculous drugs in preventing this reinfection type disease. From my own experience in the culture of resected pathology, I would expect the drugs to have little or no effect because the results of culture of primary foci from autopsy specimens are almost identical to the results of culture of resected specimens from patients with negative gastric washings.

Before deciding to treat everyone with a positive skin test, the toxic manifestations of the drugs must be weighed against their known beneficial effects. PAS has a low toxicity in children, yet I have recently seen a child with a severe reaction. Isoniazid also produces few acute toxic reactions, yet continued use of this drug may not be as harmless as we have been led to believe.

The five children who died of tuberculous meningitis varied in age from 14 months to five years—four of them were under three years old. If these children could have been treated when their skin tests converted, their deaths could have been prevented. However we did not even learn their source of infection or that their tissues were sensitized until they were admitted to our hospital. The tragic fact about these children is that they were all in general hospitals for an average of 20 days without specific therapy before the diagnosis of tuberculous meningitis was even considered and skin tests had not been done until just before admission here. The life expectancy of a child with tuberculous meningitis before specific drug therapy became available was four to six weeks from the time he became sick enough to see a physician to the time of death. Thus, the disease had almost run its course when these moribund children were started on specific treatment. In these cases, we had no opportunity to treat them as recent skin test converters and did not even have the opportunity to treat them early in their terminal tuberculous complications. Physicians have been lulled to sleep by the fall in death rate. They do not realize that the number of new cases each year and the extent of disease have not changed and that serious tuberculous disease still occurs in children.

SUMMARY

1. Primary tuberculosis is not a localized disease as is commonly thought, but has demonstrable hematogeneous dissemination in most cases. The seriousness of the disease varied with age, having a high mortality under two years of age from these hematogeneous complications. From two to five years there are still significant numbers that develop tuberculous meningitis.

2. We are finding as many new and as far advanced cases as we found five years ago. Serious tuberculosis still occurs in children.

3. Isoniazid alone will not prevent all hematogeneous complications since over ten per cent of new admissions to a tuberculosis hospital have isoniazid resistant tubercle bacilli.

4. There is no known safe drug combination that will sterilize experimentally produced tuberculosis in animals, therefore, it is not probable that we will sterilize primary lesions in people.

5. With as little as 220 days of streptomycin, PAS, and isoniazid given concurrently, it has been possible to prevent the immediate hematogeneous complications of primary tuberculosis. There is no assurance, however, that reinfection tuberculosis will not develop later.

6. A positive tuberculin test has less immunological value than previously thought because it is from original foci that reinfection type tuberculosis develops after puberty. The conversion of a skin test from positive back to negative was known to occur long before drug therapy was introduced and is no real indication that all of the tubercle bacilli are killed.

7. While our antituberculous drugs seems to be less toxic in children than in adults, serious toxic reactions occur so treatment without adequate observation is not safe.

RESUMEN

1. La tuberculosis primaria no es una enfermedad localizada como se piensa generalmente, sino que tiene una diseminación hematógena demostrable en la mayoría de los casos. La gravedad de la enfermedad varía con la edad teniendo una elevada mortalidad debajode los do años por estas diseminaciones hematógenas. De dos acinco años aún hay un número significante que desarrolla meningitis.

2. Estamos encontrando tantos casos neuvos y tantos casos muy avanzados ahora, como hace cinco años. La tuberculosis grave aún ocurre en los niños.

3. La isoniacida sola no evitará todas las complicaciones hematógenas puesto que más del 10 por ciento de las neuvas admisiones a un hospital de tuberculosos, tienen bacilos isoniacidoresistentes.

4. No se conoce una segura combinación de drogas que experimentalmente esterilice la tuberculosis provocada en los animales y por tanto no es probable que esterilice las lesiones primarias enlas personas.

5. Con tan poco como 220 días de usar estreptomicina, PAS e isoniacida simultáneamente ha sido posible prevenir las complicaciones hematógenas de la tuberculosis primaria. No hay seguridad sin embargo, de que no se desarrolle más tarde la tuberculosis de reinfección.

6. La reacción de tuberculina positiva tiene menor valor inmunobiológico de lo que antes se pensaba porque es de los focos originales que la tuberculosis de reinfección se desarrolla después de la pubertad.

La conversión de una reacción cutánea de positiva a negativase sabe que podía ocurrir mucho tiempo antes de que hubiera ladrogoterapia y no es una indicación real de que todos los bacilos tuberculosos hayan muerto.

7. Aunque nuestras drogas antituberculosas parecen ser menos tóxicas en los niños que en los adultos, occurren serias reaccionestóxicas de modo que el tratamiento sin vigilancia adecuada no es seguro.

RESUME

1. La tuberculose primaire n'est pas une affection localisée, comme on le croit généralement, mais dans la plupart des cas elle réalise une dissémination hématogène qu'on peut mettre en évidence. La gravité de

l'affection varie selon l'âge avec une mortalité élevée, chez les enfants âgés de moins de deux ans, par suite de ces complications hématogènes. De deux à cinq ans, il y a encore un nombre important d'enfants qui sont atteints de méningite tuberculeuse.

2. Nous découvrons autant de cas, et d'aussi sévères qu'il y a cinq ans. Des tuberculoses graves surviennent encore chez les enfants.

3. L'isoniazide seul n'empêchera pas toutes les complications hématogènes puisque plus de 10% des nouveaux cas admis dans un service de tuberculeux ont des bacilles isoniazido-résistants.

4. On ne connait aucune association chimiothérapique non-toxique qui puisse stériliser la tuberculose produite expérimentalement chez les animaux. Il est donc improbable que nous puissions stériliser les lésions primaires chez les êtres humains.

5. Avec un traitement aussi peu prolongé que celui fait en 220 jours par la streptomycine, le P.A.S. et l'isoniazide donnés en association, il a été possible d'empêcher les complications hématogènes immédiates de la tuberculose primaire. Cependant, nous n'avons aucune assurance que la réinfection tuberculeuse ne se développera pas plus tard.

6. Un test positif à la tuberculine a moins de valeur immunologique qu'on ne le pensait au paravant, parce que c'est à partir des foyers primitifs que la tuberculose à type de réinfection se développe après la puberté. La conversion d'un test cutané de positif en négatif était connue bien avant que la chimiothérapie fût introduite, et cela n'indique pas sans conteste que tous les bacilles tuberculeux soient tués.

7. Bien que les produits antituberculeux semblent moins toxiques chez les enfants que chez les adultes, des réactions toxiques graves peuvent apparaitre. C'est pourquoi les traitements qui ne sont pas surveillés avec précision ne sont pas sans risque.

ZUSAMMENFASSUNG

1. Die primäre Tuberkulose ist keine lokalisierte Erkrankung, wie für gewöhnlich angenommen wird, sondern besitzt in den meisten Fällen eine nachweisbare haematogene Dissemination. Die Schwere der Erkrankung ist verschieden je nach dem Alter, wobei die unter Zweijährigen eine hohe Mortalität haben zufolge dieser haematogenen Komplikationen. Zwischen 2 und 5 Jahren besteht immer noch eine beträchtliche Zahl, bei denen sich eine tuberkulöse Meningitis entwickelt.

2. Wir finden ebensoviele neue und ebensoweit fortgeschrittene Fälle, wie wir 5 Jahre zuvor fanden. Eine schwere Tuberkulose kommt immer noch bei Kindern vor.

3. INH allein wird nicht alle haematogenen Komplikationen verhüten, da über 10% der Neuzugänge eines Tuberkulosekrankenhauses gegen INH resistente Tuberkelbazillen haben.

4. Es existiert keine bekannte sichere Arzneimittel-Kombination, die bei Tieren eine experimentell erzeugte Tuberkulose sterilisiert; es ist daher

night wahrscheinlich, das wir Primärherde bein Menschen sterilisieren werden.

5. Mit nicht mehr als 220 Tagen, an denen Streptomycin, PAS and INH gleichzeitig gegeben wurden, war es möglich, die unmittelbaren haematogenen Komplikationen der Primärtuberkulose zu verhüten. Es besteht aber keine Sicherheit dafür, dass sich nicht später eine Reinfektionstuberkulose entwickeln wird.

6. Ein positiver Tuberkulin-Test hat geringeren imunologischen Wert als bisher angenommen wurde, denn es sind die Originalherde, von denen aus sich nach der Pupertät der Reinfektionstyp der Tuberkulose entwickelt. Das Vorkommen der Umkehr einer Hautprobe von einen positiven Ergebnis zurück zu einem negativen war bekannt, lange ehe die Arzneimittelbehandlung eingeführt wurde, und ist kein echter Hinweis darauf, dass die Tuberkelbazillen allesamt getötet sind.

7. Wenngleich unsere antituberkulösen Heilmittel bei Kindern weniger toxisch zu sein scheinen als bei Erwachsenen, kommen doch schwere toxische Reaktionen vor, und eine Behandlung ohne entsprechende Beobachtung ist nicht zuverlässig.

The Role of the Secondary or Precipitating Causes of Asthmatic Attacks in the Management of the Asthmatic Patient

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The importance of the secondary or precipitating causes of paroxysms in the treatment of the asthmatic patient has gained wider recognition during the past decade. Prior to the bacteriologic era and the extensive research which followed von Pirquet's classical contributions, the secondary causes of asthma received the sole emphasis by students of the disease. Thus, Hyde Salter[7] in his monograph on "Asthma: Its Pathogenesis and Treatment," published in 1860, stresses these secondary causes and particularly the reflex phenomena, which he believed to be of importance in the attacks.

It is the purpose of this paper to discuss the management of some of the secondary or precipitating causes of asthmatic paroxysms. Those which have frequently been stressed in the literature are climatic influences —changes in temperature, relative humidity and barometric pressure; acute infections of the respiratory system; physical agents—light, heat and cold; chemical and mechanical irritants; autonomic and hormonal imbalance; and psychogenic factors. Clinical experience has shown that success or failure in treatment of the nonallergic group, particularly where chronicity and intractability are manifestations, depends in no small measure, on the successful control of these secondary causes of the disease.

Primary Causes of Asthma

Allergic and Nonallergic Asthma: In the group of allergic asthmatics, the causative agents are now well understood. In them hereditary predisposition and an immunologic response characterizes this group. These patients become sensitized to inhalents, foods and drugs, and develop antibodies, which, when brought into contact with the specific antigen that has induced them, results in the allergic reaction. The designation extrinsic asthma is frequently used in the literature to refer to these allergic individuals. Bacterial and viral infections of the upper and lower respiratory tract usually play a secondary or precipitating part in bringing on paroxysms in these patients.[4]

In asthmatics past middle life, however, infections of the respiratory tract are the primary causes of recurrent attacks. The use of the term intrinsic for this group has led to some confusion.[9] The designation intrinsic for these patients implies that the cause is not allergic but due to some factor inherent in the patient's system, regardless of change of seasons, environmental exposure, occupation or diet. It has been assumed that some of the patients in this group become sensitized to their own

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bacterial decomposition products, and that their symptoms are caused by bacterial hypersensitivity or bacterial allergy.

Clinical and experimental investigations have not advanced the theory of bacterial allergy beyond the speculative stage. The induction of one form of bacterial hypersensitivity such as that due to the tubercle bacillus is well recognized and its mechanism has been studied by a number of investigators.[6] There is also experimental evidence that sensitization to streptococci play an important etiologic role in erysipelas, rheumatic fever and other infections in which streptococci are the predominative bacterial agents.[2] Bacterial sensitization as a cause of asthma is difficult to prove since skin tests with the common organisms are unreliable and corresponding antibodies have not been demonstrated with regularity. When such reactions do occur to bacterial antigens, they are rarely of the immediate type and the delayed tubercular-type reactions which may follow the injection of vaccines have little significance so far as specific etiology is concerned.

Secondary Causes of Asthma

Climate: Petersen[5] in his classic monograph on "The Patient and the Weather" quotes from the Hippocratic Text of "Airs, Waters and Places" which begins as follows: "Whoever wishes to pursue properly the science of medicine must proceed thus: First, he ought to consider what effects each season of the year can produce. The next point is the hot winds and the cold, especially those that are universal but also those that are peculiar to each particular region," and he then stresses the well-established observation that "with seasons men's diseases, like their digestive systems, suffer change." Thus, it appears that the importance of climatic factors as an influence on disease in man was recognized from the earliest times. These influences have been particularly stressed in asthma because of their well-known effect on respiration.

That excessive cold and heat are not well tolerated by the asthmatic is common knowledge. Fog and excessive humidity also predispose the patient to asthmatic attacks. Not only will such climatic factors bring on mild or severe paroxysms, but as Petersen and other clinical observers in the United States have shown, these occur frequently in the early fall and during transition from winter to spring. It is also of interest that statistical evidence shows the death rate from chronic asthma to be greater during this period.

The proper management of the asthmatic patient should include all possible measures available for control of the meteorologic environment. In general, removal of the patient to a dry, warm climate with little temperature change will usually bring about considerable improvement in his condition. However, before recommending a change of climate for the pollen-sensitive individual, the physician must be assured that the region is free of the inhalents to which the patient is sensitive. A suggested change of climate places considerable responsibility on the physician, and the patient, who, at great mental and financial hazard seeks relief through a change of climate and is not benefited thereby, may return with the psychologic set-

back which results from failure. Better and more lasting improvement is usually obtained by environmental control, with attention to heating of the home, proper ventilation, and the removal of irritating substances from the patient's home surroundings. Modern engineering techniques have made possible the creation of an artificial climate at home and at work. The better types of winter and summer air-conditioning units will give the asthmatic greater comfort during sleeping as well as during waking hours.

Antibiotics and Steroids in Asthma: It has been shown that recurrent or chronic infections of the bronchi and paranasal sinuses act as secondary or precipitating causes of attacks in allergic asthma and as primary causes in the nonallergic or infectious group. Cultures of the respiratory tract in such patients usually show a mixed growth in which Streptococcus viridans and hemolyticus, Pneumococci and Hemophilus influenzae are most frequently the predominating bacteria. Only occasionally is it possible to isolate a single organism as the sole bacteriological agent involved.

The introduction of antibiotic therapy in the control of respiratory tract infections and particularly in infectious asthma, has made possible a fundamental attack on the causative bacteria. This therapeutic weapon forged in our chemical laboratories has greatly altered not only the treatment but also the prognosis in this group.

The short-term employment of antibiotics in infectious asthma is chiefly of value in bringing an acute respiratory tract infection under speedy control. In these instances, an intramuscular injection of the tetracycline antibiotics or penicillin may be used either alone or in combination with oral medication. Penicillin, however, should be employed with caution when there is a history of sensitivity or anaphylactic reactions after a previous administration of the drug. Many patients with mild asthma may develop a chronic state or status asthmaticus without antibiotic therapy.

When antibiotics are to be administered over a long period, some knowledge of the causative bacteria is essential. Cultures and sensitivity tests, where obtainable, will aid in the selection of the appropriate antibiotic. In our experience, the combined oral use of antibiotics of the tetracycline group with penicillin covers the widest spectrum of Gram-positive and Gram-negative bacteria and gives the best clinical results. Further aid in the selection of the appropriate antibiotic for long-term therapy may be obtained by sputum cultures. Such cultures are particularly valuable because of the changing bacterial flora which may follow the use of antibiotics over long periods. If antibiotics alone do not give the desired therapeutic result, the addition of a sulfonamide drug may be necessary.

In status asthmaticus precipitated by an acute respiratory tract infection, intramuscular injections of the antibiotic should be employed. The hazard of anaphylactic reactions after an intramuscular injection of penicillin requires its judicious use.

Occasionally long-term use of antibiotics, particularly in elderly, debilitated patients, may produce symptoms due to monilial superinfection. The

gastro-intestinal distress and diarrhea resulting from monilial overgrowth may be prevented by one of the newer antibiotics which have been shown to be active against fungi.

The adrenocortical steroids are also valuable in the treatment of the asthmatic. They are helpful adjuncts to therapy because of their anti-inflammatory action and their effectiveness in tiding an asthmatic patient over an acute respiratory infection. Without their use, the paroxysm may be prolonged and lead to status asthmaticus. In this respect also, the early employment of steroid therapy as in the case of the early use of antibiotics has great prophylactic value. By this means the patient may be prevented from lapsing into a chronic and intractable state.

The introduction of the analogues of cortisone and hydrocortisone—prednisone and prenisolone—have made their use safer and less likely to produce side reactions. Disturbances in the electrolyte balance are less frequently encountered. However, the administration of adrenocortical steroids over longer periods still demands caution and careful observation. All the well-known safeguards against untoward reactions should be followed. These should include the proper selection of patients and a maintenance dose at the lowest level necessary to keep the patient symptom-free. The ulcer and hyperacidity patient, in particular, should be carefully observed. In them the addition of antacids—aluminum hydroxide and magnesium trisilicate—will frequently make possible the administration of the steroids where they would otherwise be contraindicated.

Another sequel of long-term steroid therapy which should be kept in mind is the possible atrophy of the adrenal cortex resulting from its inactivity. This can be overcome in part by simultaneous injections of adrenocorticotrophic hormone during their prolonged oral use.

Finally, it should be stressed that antibiotic and steroid therapy when used in combination at the onset of an asthmatic attack precipitated by a respiratory infection will frequently prevent chronicity and intractability. Such combined therapy will also lessen the dangers arising from masked infections.

Autonomic and Hormonal Factors in Asthma: The classic monograph of Eppinger and Hess on "Vagotonia," published in 1915, stimulated new interest in the autonomic nervous system as the great regulating and coordinating mechanism of the body. Their studies led them to conclude that the parasympathetic rather than the sympathetic was dominant in asthma. Pharmacologic investigations on adrenergic and cholinergic drugs, however, support the view that the myogenic activity of smooth muscle, in general, and bronchial musculature in particular, is regulated by the characteristic double innervation of the autonomic nervous system. This concept would explain also the therapeutic value of the newer anticholinergic drugs as effective parasympathetic or vagal blocking agents in the control of asthmatic paroxysms.[8]

Studies on the pathologic physiology of asthma suggest, moreover, that bronchoedema also plays an important role in the decreased ventilation capacity observed in the asthmatic patient.[2]

The relation of the endocrine glands to autonomic nervous system and their influence on the asthmatic state has been the subject of speculation since the isolation of adrenalin from the adrenal medulla over a half century ago. Urbach and Gottlieb in their stimulating textbook on allergy[10] discuss this problem in relation to allergic phenomena.

Renewed interest in the role of the hormones in asthma was stimulated by the research of recent years on the part played by the adrenal cortex and the pituitary gland in the elaboration of adrenal cortical steroids. Clinical observation supports the view that adrenal steroids are valuable anti-inflammatory agents and that they may possibly produce therapeutic effects through the mediation of the autonomic nervous system. It is, therefore, obvious that appropriate pharmacotherapy and the judicious employment of the steroids are among the most useful measures in the control of autonomic imbalance and its effect on the asthmatic state.

Psychogenic Influences: Centuries ago Socrates with his profound insight must have had in mind the psychosomatic approach to the treatment of disease when he admonished: "Let no one persuade you to cure him until he has given you his soul to be cured, for this is the great error of our day in the treatment of the human body, that physicians separate the soul from the body."[5]

The revival of interest in psychosomatic medicine in recent years has placed more emphasis on the psychogenic factor in asthma. One need not stress the significance of psychodynamic influences on body function. These are well recognized in many chronic diseases such as those affecting the gastrointestinal, circulatory, urinary and respiratory systems. Although there is no clinical evidence that psychic factors alone without allergy, infection, or both can cause asthma,[12] they may be among the most potent factors in precipitating a paroxysm or modifying the disease to the extent that the asthmatic condition becomes chronic and intractable. The beneficial therapeutic effect that an adjustment to life situations has on an asthmatic patient, and the relief obtained after correction of anxiety states are so often observed that they cannot be overlooked.

The psychotherapeutic management of a patient with asthma differs only in minor details from that applied in the psychotherapy of any disease with a tendency to chronicity. An anxious, depressed, dependent, and phobic patient will naturally have a more violent emotional response to recurring attacks of asthma than one, who, when in good health has shown emotional stability and normal adjustments to life situations.

Every understanding physician is well aware of the psychotherapeutic problem of the asthmatic patient. Much of what he may do is inherent in the doctor-patient relationship. In the majority of instances, the physician who treats the organic causes underlying a patient's asthmatic condition is best able to minister to his psychotherapeutic needs. In the milder anxiety and phobic states, the newer tranquilizing drugs have been found of great value in treatment. Where the situation demands the more specialized techniques, the physician should refer the patient to a cooperative psychiatrist who is qualified by training to know the significance of the

psychologic stresses which give rise to such emotional responses as anxiety, fear, resentment, hostility, frustration, rivalry and guilt.

The physician who fails to minister to the emotional problems of his asthmatic patient cannot, therefore, hope to achieve worthwhile therapeutic success.

Physiotherapy in Asthma: In asthma, the degree of emphysema which develops and its reversability or irreversability depends largely on the chronicity of the condition. In the less severe and less chronic forms of asthma, an asthmatic paroxysm causes only temporary over-distention of the lungs which return to normal after the attack. The resulting emphysema is not associated with irreversable changes in the thorax and lungs and may be designated as functional emphysema. It is in these milder forms of lung distention and impaired pulmonary ventilation that breathing exercises have great therapeutic value. The importance of physical methods of improving respiration were first stressed by the Asthma Research Council of London more than 20 years ago.[1] The purpose of these exercises is to encourage diaphragmatic breathing in order to improve the excursion of the lower ribs and diaphragm and thereby restore the lungs and thorax to a comparatively normal state.

SUMMARY

Allergy, infection of the upper and lower respiratory tract and allergy with superimposed infection are now considered by most clinical observers to be the primary causes of asthma.

Therapy directed to these causes alone will not, in most instances, bring about successful results. Experience has shown that success or failure in treatment, particularly of the nonallergic group of patients, where chronicity and intractability may be present depends on the effective control of the secondary or precipitating causes of the attacks.

The secondary causes which have been chiefly stressed in the literature are climatic influences, physical agents—light, heat and cold; chemical and mechanical irritants; acute infections of the respiratory system; autonomic and hormonal imbalance and psychogenic factors.

In most instances, the employment of antibiotics and adrenal corticosteroids, either alone or in combination, will tide an asthmatic patient over an acute paroxysm precipitated by an infection of the respiratory tract. These therapeutic agents, used in small maintenance doses, also have prophylactic value in lessening the tendency toward chronicity and intractability.

Other valuable adjuncts to effective therapy are breathing exercises to improve pulmonary ventilation and thereby lessen the tendency to emphysema, the removal of chemical and mechanical irritants, the correction of autonomic and hormonal imbalance, and lastly, a proper therapeutic approach to the emotional problems of the asthmatic patient.

RESUMEN

La alergia, la infección de las vías respiratorias altas y alergia con infección añadida, se consideran ahora por la mayoría de los clínicos como las causas primarias del asma.

La terapéutica dirigida a estas causes solas en la mayoría de los casos no produce satisfactorios resultados.

La experiencia ha demostrado el éxito o el fracaso en el tratamiento especialmente en el grupo no alérgico donde puede haber cronicidas y falta de respuesta dependen del control efectivo delas causas secundarias o precipitantes de los ataques.

Las causas que se han señalado especialmente en la literatura, son las influencias climáticas, luz, calor y frío; irritantes químicos y mecánicos; infecciones agudas del aparato respiratorio; descompensación del sistema autónomo y del hormonal así como factores psicógenos.

En la mayoría de los casos el empleo de los antibióticos y da los corticesteroides adrenales, ya sea solos o en combinación, ayudarán a sortear el paroxismo agudo de un asmático precipitado por una infección de las vías respiratorias. Estos agentes terapéuticos usados en dosis pequeñas de mantenimiento también tienen valor profiláctico para atenuar la tendencia hacia la cronicidad y la resistencia al tratamiento.

Otros adjuntos valiosos para la terapia efectiva son los ejercicios respiratorios para mejorar la ventilación pulmonar y así amenguar la tendencia al enfisema, la exclusión de irritantes mecánicos y químicos, la corrección del desequilibrio autónomo y hormonal y por último una atención adecuada a los problemas emocionales del asmático.

RESUME

L'allergie, l'infection de l'arbre respiratoire supérieur et inférieur, et l'allergie compliquée d'infection sont maintenant considérées par la plupart des cliniciens comme les causes essentielles de l'asthme.

Le traitement dirigé seulement contre ces causes n'apportera pas, dans la plupart des cas, des résultats vraiment satisfaisants. L'expérience a montré que le succès ou l'échec du traitement, particulièrement lorsqu'il s'agit du groupe de malades non-allergiques où la chronicité et l'incurabilité peuvent exister, dépend de la possibilité de juguler les causes secondaires qui ont déclanché les attaques.

Les causes secondaires qui ont été brièvement mises en lumière dans la littérature sont: les influences climatiques, les agents physiques (lumière, chaleur, froid), les irritants chimiques et mécaniques, les infections aiguës du système respiratoire, le déséquilibre autonome et hormonal et les facteurs psychiques.

Dans la plupart des cas, l'emploi des antibiotiques et des produits surrénaliens cortico-stéroïdes, soit seuls, soit en association, débarrassera un malade asthmatique d'une crise aiguë déclanchée par l'infection de l'arbre respiratoire. Ces agents thérapeutiques, utilisés en petites doses d'entretien, ont aussi une valeur prophylactique en diminuant la tendance à la chronicité et l'incurabilité.

D'autres adjuvants de valeur à la thérapeutique efficace sont les exercices respiratoires, pour améliorer la ventilation pulmonaire, et diminuer la tendance à l'emphysème, la suppression des irritants chimiques et mécaniques, la correction du déséquilibre autonome et hormonal, et enfin un effort de traitement de l'état émotionnel du malade asthmatique.

ZUSAMMENFASSUNG

Allergie, Infektion der oberen und unteren Luftwege und Allergie mit aufgepfropfter Infektion werden jetzt von den meisten klinischen Boebachtern als die primären Ursachen des Asthmas angesehen.

Eine auf diese Ursache allein gerichtete Therapie wird in den meisten Fällen keine erfolgreichen Resultate bringen. Die Erfahrung hat gezeigt, das Erfolg oder Versagen bei der Behandlung, besonders in der nichtallergischen Gruppe von Patienten, bei denen ein chronischer Krankheitszustand und Unbeeinflussbarkeit vorliegen können, abhängt von der wirksamen Beherrschung der sekundären oder auslösenden Ursache der Anfälle.

Die sekundären Ursachen, die hauptsächlich in der Literatur hervorgehoben wurden, sind: Klimatische Einflüsse, Naturkrägte—Licht, Hitze and Kälte; chemische und mechanische Reizmittel; akute Infektionen der Atmungsorgane; autonome und hormonelle Gleichgewichtsstörungen und psychogene Faktoren.

In den meisten Fällen wird die Anwendung von Antibiotizis und Cortiko-Steroiden, sei es allein oder in Kombination, einem asthmatischen Patienten über einen akuten Krampf hinweghelfen, der durch eine Infektion der Atmungsorgane ausgelöst wurde. Diese therapeutischen Stoffe haben auch bei Verwendung in kleiner erhaltungsdosis einen prophylaktischen Wert durch Verringerung der auf einen chronischen Krankheitszustand und Unbeeinflussbarkeit gerichteten Tendenz.

Andere wertvolle Hilfsmittel für eine effektive Therapie sind Atemübungen zur Verbesserung der Lungenbelüftung und damit zur Verringerung der Neigung zum Emphysem, zur Entfernung der chemischen und mechanischen Reizmittel, zur Korrektur der autonomen und hormonellen Gleichgewichtsstörungen und schliesslich ale ein geeigneter therapeutischer Weg zu dem emotionellen Problem des asthmatischen Patienten.

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Comparative Efficacy of the Concurrent Use of Pyrazinamide and Isoniazid with That of Other Forms of Therapy in the Treatment of Pulmonary Tuberculosis*

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Introduction

In 1952 the clinical use of pyrazinamide (PZA) was first reported by Yeager, Munroe, and Dessau[1]. In 1954 McCune, Tompsett, and McDermott[2] observed that the combined use of isoniazid and pyrazinamide in the treatment of pulmonary tuberculosis was especially effective. Isoniazid (INH) and pyrazinamide have been employed at the San Fernando Veterans Administration Hospital since 1952, but not until 1954 was such therapy compared with other forms of treatment for tuberculosis.

Method of Procedure

Patients with streptomycin-sensitive strains of *M. tuberculosis* requiring therapy were treated with one of the following combinations of antituberculosis drugs.

1. Isoniazid, 300 mgm. daily, with pyrazinamide, 3 gm. daily.
2. Streptomycin, 1 gm. twice per week, with para-aminosalicylic acid, 12 gm. daily.
3. Streptomycin, 1 gm. twice per week, with isoniazid, 300 mgm. daily.
4. Isoniazid, 300 mgm. daily, with para-aminosalicylic acid, 12 gm. daily.

No selection of patients was made other than by the use of the last digit of the hospital registration number which indicated the therapeutic regimen to be administered.

Patients with streptomycin-resistant organisms were treated in a special group with isoniazid and pyrazinamide employing the above dosages. They were treated from five to 17 months with their respective types of therapy. The number treated in each group and the extent of tuberculosis observed prior to therapy are recorded in Table I. It will be noted that those in the four groups with streptomycin-sensitive organisms presented approximately the same extent of tuberculous disease. On the other hand, in the majority with streptomycin-resistant organisms the disease was far advanced.

Results

The sputum from nine of 10 patients with streptomycin-sensitive *M. tuberculosis* treated with pyrazinamide and isoniazid became bacterio-

*Patients treated at the San Fernando VA Hospital, San Fernando, California.
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logically negative. In only one in this group did the sputum fail to convert from positive to negative. Furthermore, the rapidity of conversion was greater than that observed with the other types of therapy.

In 12 patients with sputum containing streptomycin-resistant *M. tuberculosis* treatment with pyrazinamide and isoniazid was less effective. In only four cases did the sputum convert from positive to negative. Thus from the bacteriologic point of view the forms of therapy other than pyrazinamide and isoniazid were superior. See Table II.

Radiologically patients treated with pyrazinamide and isoniazid failed to show the degree of improvement observed after treatment with streptomycin and para-aminosalicylic acid, streptomycin and isoniazid, and with isoniazid and para-aminosalicylic acid. Only two of 13 showed marked improvement by x-ray film. Five showed no improvement even after extended therapy. Generally when the patient showed radiologic signs

TABLE I

GROUPING OF PATIENTS AND EXTENT OF TUBERCULOUS DISEASE

Therapy	Patients	Extent of Tuberculosis		
		Minimal	Moderate	Far Advanced
PZA+INH	13	3	7	3
SM+PAS	16	1	11	4
SM+INH	12	2	7	3
INH+PAS	5	1	1	3
PZA+INH	12*		3	9
TOTAL	58	7	29	22

*Infected with streptomycin-resistant *M. tuberculosis.*

TABLE II

RESULTS OF BACTERIOLOGIC STUDIES FOR M. TUBERCULOSIS ON SPUTUM AND GASTRIC WASHINGS

Therapy	Pretreatment Bacteriology			Conversion in Months After Initiating Therapy								
	Neg.	Pos. Smear and Culture	Pos. Culture Only	0	1	2	3	4	7	8	14	Con't. Pos.
PZA+INH	3	1	9	2	6		1					1
SM+PAS	6	5	5		7	1			1			1
SM+INH	6	3	3	1	2		3					0
INH+PAS	1	2	2		2					1	1	0
PZA+INH*	1	8	3		1		2	1				7

*Infected with streptomycin-resistant *M. tuberculosis.*

of progress, the rate of improvement was slower with pyrazinamide and isoniazid than with the other methods of treatment. See Table III.

Toxicity requiring cessation of therapy occurred only with pyrazinamide and isoniazid. In the group of 58 patients seven treated with pyrazinamide and isoniazid showed the following complications: Two had hepatitis and one each suffered from abnormal liver function tests, neuritis, nausea and anorexia. In one patient with a strain of streptomycin-sensitive *M. tuberculosis* prior to therapy the organism became pyrazinamide-resistant. See Table IV.

Three who failed to improve completely with pyrazinamide and isoniazid required lung resections. Smears for acid fast bacilli were obtained from resected tissue from each patient. Culture and guinea pig inoculations from the material obtained from two receiving 17 and seven months of therapy respectively were negative. The cultures and guinea pig inoculations from the resected tissues of the third patient who received 10 months of therapy were positive. In view of statements by McDermott[2] that pyrazinamide and isoniazid therapy sterilized the tuberculous lesions the positive findings are of interest.

TABLE III

RESULTS OF X-RAY EXAMINATIONS

		Improved		Unimproved	
Therapy	Patients	Moderately	Markedly	Unchanged	Worse
PZA+INH	13	6	2	5	0
SM+PAS	16	8	4	4	0
SM+INH	12	6	6	0	0
INH+PAS	5	2	2	1	0
PZA-INH	12*	4	2	5	0
TOTAL	58				

*Infected with streptomycin-resistant *M. tuberculosis*.

TABLE IV

COMPLICATIONS IN 25 PATIENTS TREATED WITH PZA AND INH REQUIRING CESSATION OF USE OF PZA

Hepatitis	2
Abnormal Liver Function Tests	1
Neuritis	1
Nausea	1
Loss of Appetite	1
PZA Resistance of *M. Tuberculosis*	1
TOTAL Patients	7

SUMMARY

1. Fifty-eight patients with pulmonary tuberculosis were treated in five random groups to evaluate therapeutic efficacy of pyrazinamide and isoniazid.

2. Pyrazinamide and isoniazid therapy was slightly more effective in causing bacterial conversion of sputum from patients with streptomycin-sensitive *M. tuberculosis* than combinations of streptomycin and para-aminosalicylic acid, streptomycin and isoniazid, and isoniazid and para-aminosalicylic acid. In addition the conversion of sputum from positive to negative took place somewhat more rapidly with pyrazinamide and isoniazid than with the other forms of treatment.

3. Improvement as recorded by x-ray films was less rapid with pyrazinamide and isoniazid than with the use of the other treatment schedules.

4. Toxicity of pyrazinamide and isoniazid was greater than that obtained with streptomycin and isoniazid, streptomycin and para-aminosalicylic acid, and with isoniazid and para-aminosalicylic acid.

RESUMEN

1. Cincuenta y ocho enfermos de tuberculosis pulmonar se trataron en cinco grupos sorteados para valuar la eficacia terapéutica de la pirazinamida y de la isoniacida.

2. El tratamiento con pirazinamida e isoniacida es ligeramente más eficaz par obtener la conversión bacteriana en los esputos de enfermos con micobacteria tuberculosa sensible a la estreptomicina que las combinaciones de estreptomicina PAS, estreptomicina INAH y la de INAH-PAS. Además, la conversión de esputos a negativos fué algo más rápida con PZA-INAH que con las otras formas de tratamiento.

3. El mejoramiento según las radiografías fué menos rápido con PZA-INAH que con el uso de los otros tratamientos.

4. La toxicidad de la PZA-INAH fué mayor que la de SM-INAH, SM-PAS y que INAH-PAS.

RESUME

1. Pour évaluer l'efficacité thérapeutique do la pyrazinamide et de l'isoniazide, 85 malades tuberculeux pulmonaires furent répartis arbitrairement en cinq groupes.

2. Le traitement par la pyrazinamide et l'isoniazide, en parvenant à négativer l'expectoration de malades porteurs de germes sensibles à la streptomycine, fut légèrement plus efficace que les associations de streptomycine et de P.A.S., de streptomycine et d'isoniazide, et d'isoniazide et de P.A.S. En outre, la négativation des crachats se montra un peu plus rapide avec l'association pyrazinamide-isoniazide qu'avec les autres formes de traitement.

3. Envisagée du point de vue radiologique, l'amélioration fut moins rapide avec la pyrazinamide et l'isoniazide qu'avec l'emploi des autres modalités de traitement.

4. La toxicité de la pyrazinamide et de l'isoniazide associées fut plus grande que celle obtenue avec l'association streptomycine-isoniazide, streptomycine-P.A.S. et isoniazide-P.A.S.

ZUSAMMENFASSUNG

1. Es wurden 58 Kranke mit Lungentuberkulose in 5 zufälligen Gruppen behandelt zur Bestimmung der therapeutischen Wirksamkeit von Pyrazinamid und INH.

2. Pyrazinamid und INH—Behandlung war von etwas besserer Wirkung hinsichtlich des Zustandeskommens eines bazillenfreien Sputums bei Kranken mit gegen Streptomycin empfindlichen Tuberkelbazillen als die Kombinationen von Streptomycin und PAS, Streptomycin und INH und INH und PAS. Darüber hinaus erfolgte die Bazillenfreiheit des Sputums etwas schneller mit Pyracinamid und INH als bei den anderen Behandlungsarten.

3. Rückbildungen, wie sie anhand von Röntgenbildern zu verzeichnen waren, gingen weniger rasch vonstatten mit Pyrazinamid und INH als bei Verwendung der anderen Behandlungs-Schemata.

4. Die Toxizität von Pyracinamid und INH war grösser als diejenige die bei Streptomycin und INH vorkam oder bei Streptomycin und PAS, und bei INH und PAS.

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Case Report Section

A Case of Benign Inoculation Lymphoreticulosis Presenting as Axillary Lymphadenopathy of "Obscure" Origin

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While the classic or current causes of enlarged axillary lymph nodes are well known and immediately sought, the more unusual ones are occasionally overlooked.

Among the recently described nosographic entities there is one that appears to be fairly common, and most likely more frequent than the hundreds of cases so far described[1, 2] in literature, both in this country and abroad, would seem to indicate; for its clinical manifestations are ostensibly protean,[1] its course usually mild, and hence not too conducive to an intensive diagnostic investigation[2, 3] and, finally, its main etiologic factor, a virus of the lymphogranuloma-ornithosis type, easily and universally transmissible by its main, "ecumenic" host, the cat.[4, 5, 6] This is "cat-scratch disease," also known as benign inoculation lymphoreticulosis. While it is most frequently caused by cat-scratch, or bite,* the rabbit, the porcupine and most likely other mammals, occasionally transmit it. Minor trauma caused by thorns, wood splinters etc. (perhaps soiled by infected animals' urine) also play a role in its transmission, in some reports[2] accounting for about 8 per cent of cases.

Usually, a few days after a cat-scratch, the injured organ, most commonly a hand or a leg of a youngster, presents a papule surmounted by a vesicle or pustule which frequently ulcerates. One to three weeks later, the regional lymph nodes become swollen, and sometimes suppurate. All of the lesions may remain indolent, and the systemic reaction is practically nil. However, fever, severe malaise, generalized maculo-papular rash and even mild encephalitis develop occasionally. Also, several instances of oculo-glandular syndromes (Parinaud's type) have been observed. Nonetheless, the ultimate prognosis apparently is good. The blood picture usually is unaffected, but the sedimentation rate frequently is accelerated.

In the absence of history of a scratch or bite, the clinical picture may become extremely confusing. Sometimes no history of trauma can be elicited.[1, 2, 5]

Case Report: A 12 year old Puerto Rican boy was examined with the exclusive complaint of a "lump" in his left axilla, painful only on lifting the arm, of about two weeks duration.

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*For other complications of cat bites, see ref. 4.

The personal and the family history were noncontributory. Search for contact with animals and a skin lesion was unrevealing. There was no history of fever, chills or malaise antedating the appearance of the axillary lesion.

Physical examination revealed a protuberance in the left axilla the size of a walnut. The remainder of the physical examination was negative. He was afebrile and felt well. Routine laboratory examinations including urine analysis, complete blood count, and roentgenogram of the chest, were normal. Blood serology and two cultures were negative.

During the next few days the lymphadenopathy seemed to increase. Tuberculosis or lymphomas were considered as main diagnostic possibilities.

Dr. E. Schnebel, Parkchester General Hospital, removed the mass which consisted of enlarged, soft lymph nodes. On further exploration of the armpit three more enlarged lymph nodes were found and removed.

On section, the nodes showed pinkish tan soft parenchyma. Histologically there were many areas of reticulum cell proliferation and focal necrosis suggesting benign infectious granuloma, "possibly cat scratch disease."

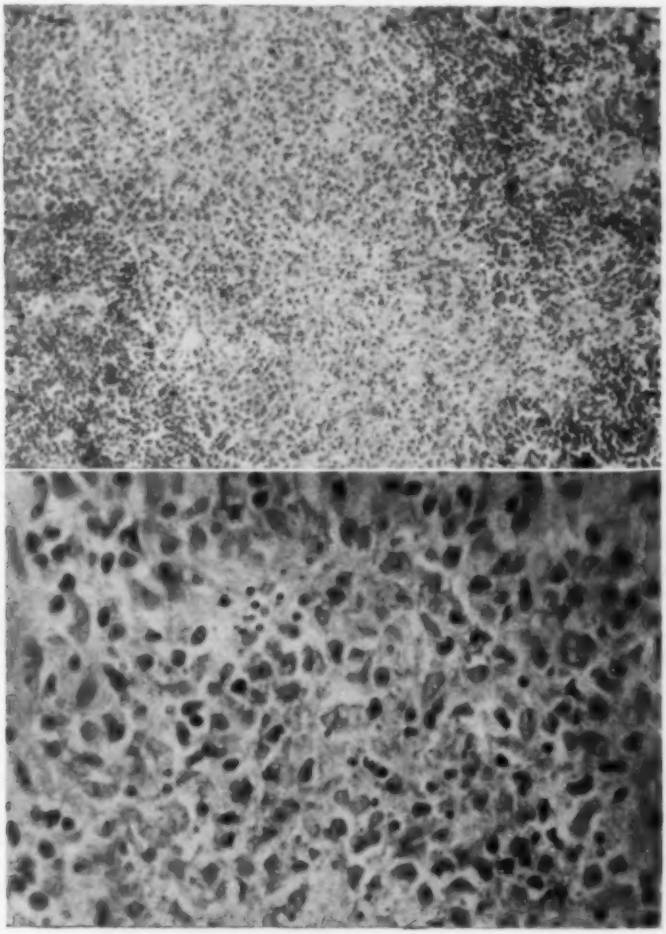

FIGURE 1

FIGURE 2

Figure 1: Hyperplasia of reticulum cells. H and EX x 125.—*Figure 2:* Area of early necrosis, showing nuclear débris and inflammatory cells. H and EX x 250.

Figure 1 shows marked hyperplasia of the reticulum cells forming small and large ill-defined foci. On the other hand, the central areas of some of these collections showed (Fig. 2) an early necrosis with mild infiltration by polymorphonuclear leukocytes and plasma cells. Nuclear débris was also noted.

Patency of the peripheral sinuses of the lymph nodes and moderate increase of their germinal centers were observed. The capsule showed perivascular lymphocytic infiltration.

These unexpected microscopic findings led to further investigations. On closer questioning, it was learned that the boy frequently played with a neighbor's cat which occasionally slept with him but no scratch or bite was admitted. An intradermal test was done with an antigen from a necrotic lymph node of a proved case of cat-scratch disease. The 48, 72 and 96 hour readings were intensely positive. The test was repeated with a similar antigen from another proved case with similar result. Simultaneously, a non-specific antigen was employed (obtained from a lymph node from another patient suspected of, but not having the disease), and the result was negative.*

Several authors, especially Daniels and MacMurray, Kalter and associates,[2] and more recently Armstrong and his associates[3] have emphasized the protean nature of this disease's clinical picture and the great diagnostic value of the skin test. The present case indubitably confirms these statements.

I am grateful to Dr. Grishman for her pathologic examination of the excised material, and to Dr. R. Garret for his help in the securing and interpretation of the microphotographs.

*I am deeply indebted to Dr. C. Sprunt who kindly supplied me the antigens.

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Metastasizing (Malignant) Bronchial Adenoma with Heteroplastic Bone Formation

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Almost five decades ago (1907) Von Eichen, with the aid of a bronchoscope, diagnosed and removed a benign neoplasm of the bronchus. Until now, the management of bronchial adenomas (which comprise approximately 10 per cent of all broncho-pulmonary neoplasms) has posed a problem to the clinician and pathologist alike because of their peculiar morphology, unusual growth pattern and the tendency for some to metastasize.

The terminology of this disease entity is, to say the least, varied and confusing. Mallory[1] considered adenoma a poor term for these tumors because they do not consistently form glands; however, the failure of these tumors to show acinar differentiation does not negate the use of the term adenoma. Doty[2] suggested that the term "adenoma" be reserved for the group as a whole and that "carcinoid adenoma" and "mixed tumor adenoma" be used for classifying the histologic types. More recently the term adenoid cystic adenoma has come into favor as a designation for the "mixed-tumor adenoma" and because of the high incidence of metastasis (25 to 30 per cent) some authors group this lesion with the carcinomas.

Morphologically, these tumors resemble carcinoids of the intestinal tract, but they may be differentiated by the following characteristics:

1. Granules in the cells of bronchial adenomas are not blackened by ammoniacal silver nitrate.

2. Cells of bronchial adenomas often contain some mucus that is stained by mucicarmine, but gastro-intestinal carcinoids do not.

3. Occasionally, "onkocytes" are present in bronchial adenomas. These cells are present in the mucous and serous glands and ducts of the bronchi of the adult, but not in the bronchi of the fetus.

4. In addition to the above mentioned features which Hamperl[3] set forth, Stout[4] has added this characteristic: that bronchial adenomas have an extremely vascular stroma and bleed freely and repeatedly.

Histologically and clinically, the majority of these neoplasms are benign, but a review of all the reported cases by McBurney, Kirklin, and Woolner[5] in 1953 revealed that approximately 10 per cent of all bronchial adenomas metastasized to regional lymph nodes and/or distant organs. The "mixed tumor" adenomas are more likely to show pleomorphism and tend to metastasize more frequently.

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Bone formation, while not a rarity in this type of neoplasm, occurs rather infrequently. Holley[6] reported finding bone in eight of 39 cases. This is usually the result of metaplastic change in the bronchial cartilage, but it has also been shown to arise from the fibrous septa of the tumor (Mallory[1]).

Case Report

A. E., a 31 year old married white woman was admitted to the United States Army Hospital at Fort Leonard Wood, Missouri, on February 3, 1955 because of an upper respiratory infection and x-ray film evidence of a pneumonic infiltration in the right lung. She stated at this time that she had had recurrent episodes of pneumonia in the lower part of the right lung for the past five years. Physical examination revealed rales over the right side of the chest. Skin tests for coccidiodomycosis and histoplasmosis were negative, but the first dose of PPD for tuberculosis was reported positive. She was discharged afebrile on February 9, 1955 to be followed in the Out-Patient Clinic. Repeated examinations disclosed the presence of wheezes and coarse rales over the lower part of the right side of the chest posteriorly, with altered voice and breath sounds. In addition, she complained of non-productive cough, aching and a "throbbing sensation" in her right chest and a weight loss of 30 pounds by October 24, 1955, at which time she was readmitted to the hospital for evaluation of a persistent x-ray shadow casting lesion in the right lung. Skin tests were repeated, and all were reported as negative at this time. All laboratory tests were essentially normal and gastric washings were negative for acid-fast bacilli. Serial x-ray films over the past year showed a right hilar mass present in all films (Figure 1). On October 31, 1955 bronchoscopy disclosed a large intrinsic mass, with an irregular surface projecting into the lumen of the right bronchus 1.0 cm. distal to the upper lobe bronchus and situated on the posterior wall. Only a portion of the middle lobe orifice could be visualized and none of the lower lobe orifice could be seen. A biopsy was taken and a catheter introduced for instillation of some radio-opaque material. Subsequent bronchograms showed good filling of the middle lobe and no contrast medium in the lower lobe (Figure 2). Pathologic diagnosis of the biopsy material was bronchial adenoma, carcinoid type.

On November 8, 1955 she was explored by Captain James B. Dumm. The tumor was situated in such a way that it necessitated a middle and lower lobectomy rather

FIGURE 1

FIGURE 2

Figure 1: Posterior-anterior roentgenogram of the chest taken in September 1955, two months prior to surgery. There is a knob-like projection off the right hilus with small foci of increased density within it. The peribronchial markings of the right base are accentuated—*Figure 2:* Posterior-anterior view of the chest following instillation of contrast medium into the bronchial tree (October 1955). Note the incomplete filling of the right middle and lower lobes. This film was made at the time of bronchoscopy and biopsy of the tumor mass.

than limited resection and a bronchial plastic procedure. In the process of dissecting the tumor free, an abscess in the region of the interlobar fissure was broken into and its contents were spilled into the right chest cavity. After the lobes were removed, the line of excision on the bronchial stump was seen to be involved with tumor tissue, so a few millimeters more of bronchus was removed before the stump was closed. Surgery was completed after four hours, and the patient had an uneventful recovery.

The resected specimen consisted of the right middle and lower lobes which had been fixed in formaldehyde solution. The pleura showed some blue-black pigmentation and a broad fibrous adhesion which partially obliterated the interlobar fissure. The middle lobe was 12.0 x 8.0 x 3.0 cm. and the lower lobe, 15.0 x 10.0 x 3.5 cm. The wall of the bronchial stump varied in thickness from 0.15 to 1.0 cm. because of a large tumor mass which almost completely obliterated the lumen (Figure 3). At one point the tumor mass extended 1.2 cm. lateral to the bronchus. The peribronchial lymph nodes were slightly enlarged and pigmented blue-black.

Upon opening the bronchus, a tumor mass was encountered projecting into the lumen and almost completely obstructing the passage to the lower lobe. The lesion had an oval configuration with a fairly even surface which was partially covered by a friable yellow-gray membrane.

Surfaces made by cross-sectioning at different levels were of yellow-gray to grayish-brown color and the central portion of the mass cut as though it were calcified. In the superior segment of the lower lobe, there was an abscess cavity which was devoid of contents. A dilated bronchus formed one wall of this abscess. A few stellate fibrotic areas were noted throughout the parenchyma of the lower lobe.

Sections through the bronchus at various levels showed a circumscribed tumor mass replacing most of the bronchial wall and extending into the parenchyma of the lung. The tumor was made up of pale cells with centrally placed, round, vesicular nuclei and fairly distinct cell borders. There were many thin fibrous septae coursing through the tumor. The bronchial cartilages were still intact, but in some areas were surrounded by osseous tissue. The osseous tissue appeared to be derived from the cartilage except for some far removed fragments which bore no relation to it (Figure 4). Practically all the marrow spaces were filled with tumor cells. The lesion contained many sizable vascular spaces. Of the several lymph nodes present, one showed a circumscribed nest of tumor cells similar in appearance to the adenoma proper. One node attached to

FIGURE 3: Gross photograph of the resected specimen with the proximal portion of the bronchus removed. Note how the tumor filled the lumen of the bronchus, replaced preexisting structures and extended peripnerally into the lung parenchyma.

the periphery of the tumor showed no evidence of invasion. The pathologic diagnoses were: (1) right bronchus intermedius, adenoma (carcinoid type); (2) right lower lobe, bronchiectatic abscess; (3) peribronchial lymph node, metastatic adenoma; and, (4) heteroplastic bone formation within the bronchial adenoma.

Discussion

This case exemplifies the potentialities of a bronchial adenoma—not only does it endanger the patient's life because of its malignant tendencies, but the chronic bronchial obstruction is responsible for the repeated bouts of pneumonia and, eventually, the development of irreversible bronchiectatic changes. Also, one cannot minimize the bleeding tendencies of these neoplasms.

The prognosis in this case is guarded. The finding of a metastatic focus in one of the peribronchial lymph nodes leads one to believe that there may be other metastatic lesions which were not recognized at the time of surgery. Especially since this metastatic node was quite removed from the tumor proper and not the result of direct extension.

Heteroplastic bone formation in bronchial adenomas takes origin from the bronchial cartilage or the connective tissue stroma of the tumor. So in this particular case where the spicules of bone are found among tumor cells quite removed from bronchial cartilage, we are of the opinion that the origin of the bone was from connective tissue. Holley[6] found bone in eight of the 39 cases of bronchial adenoma he studied; it was evident in three of the eight cases that the bone arose from the connective tissue. Because of the degree of bone formation present in this tumor, it cut with difficulty and required decalcification before sectioning. Many of the marrow spaces however, were filled with tumor cells. By carefully examin-

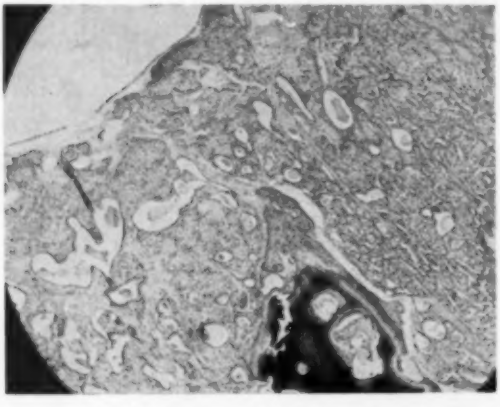

FIGURE 4: Low power field showing bronchial wall replaced by the bronchial adenoma. There is a layer of intact epithelium lining the bronchus and an edematous basement membrane. Several glandular spaces partially filled with mucus are seen. Fibrous septae and a large mass of bone are noted. H. & E. x 40.

Illustrations for Figures 1 and 2 courtesy of the Municipal Tuberculosis Sanitarium, Chicago, Illinois.

Illustrations in Figures 3 and 4 courtesy of Armed Forces Institute of Pathology.

ing the chest roentgenograms one can see an area of increased density in the hilar mass which is most likely attributable to the bone formation. Over-exposure of the roentgenogram might have made this more evident. While in the past we have been inclined to think of calcified and/or ossified foci as representing benign processes when seen on x-ray films this case is an exception that stresses the need for modifying our evaluation of such lesions.

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Editorial

Diagnostic X-Rays of the Chest—A Possible Hazard?*

The growing realization, particularly in the last few years, that ionizing radiation is potentially dangerous to gonads and bone marrow, has led to a certain degree of soul-searching by radiologists, internists, and others concerned in exposing their patients to diagnostic and therapeutic x-ray procedures. It is important that this soul-searching continue, for there can be no doubt that x-ray therapy for non-neoplastic disease, notably for spondylitis, has led to leukemia in some cases, and by inference other therapeutic x-ray procedures, as for chronic dermatitis, bursitis, etc., must now be carefully assessed. Even the uncontrolled use of diagnostic x-rays must be given careful consideration.

In a society as highly cultured and affluent as our own, with ready access to medical, hospital, and laboratory facilities, there is indeed cause to examine our current practice and see whether it needs modification. There can be no doubt that many drugs, chemicals, and other substances are often used with but little indication; some of them are potentially, if not actually harmful. Similarly, many unnecessary laboratory tests are carried out. Although most of them are relatively harmless, except possibly to the pocketbook, diagnostic x-ray procedures represent a demonstrably potent and potentially harmful force. Without of course sacrificing essential diagnostic aids, it behooves us to post a sign of caution.

In the current propaganda for periodic physical examinations, diagnostic x-rays play a large role. Of these, the most important by far is the chest x-ray film which has become a routine procedure, whereas—except among the most rabid examiners—gastro-intestinal series, intravenous urography, barium enemas, and the like are reserved for those individuals having symptoms relative to these areas. It is good to realize that a diagnostic x-ray film of the chest need not irradiate the individual with more than a milliroentgen or two, whereas a roentgenologic survey of the gastro-intestinal tract—with fluoroscopy—might expose the individual to 15 to 25 roentgens; x-rays of the spine with lateral films 9-12 roentgens; and of the pregnant woman for position of the fetus 5 to 15 roentgens. In contrast with these relatively large doses, the rapid-exposure diagnostic x-ray film of the chest appears quite safe.

Leukemia, which from all accounts has been on the increase decade by decade in the past 30 years, probably has several diverse etiologies, but of them all, the only one which has been thoroughly documented in humans is that of ionizing radiation. The increasing incidence of leukemia may be said to run parallel with the increasing use of ionizing radiation in medical

*Aided by a grant from the Atomic Energy Commission (Contract: AT (30-1) 1276).

practice. Merely because the parallel exists does not, of course, constitute proof that the increased incidence is due to the increasing use of radiation. On the other hand, since an etiologic relationship is known, it is important to re-examine with care all our various diagnostic x-ray procedures, notably "routine" and unnecessary filming and the use of fluoroscopy when fast exposure x-rays can be used. Some patients with tuberculosis or some other chest lesion are x-rayed every month, two, or three; and with not merely one x-ray film but many. I have recently seen a young woman with acute leukemia in whom there was a history of many series of x-ray examinations of the chest for suspected tuberculosis over a period of 10 years. This was probably coincidental, but the possibility that coincidence was *not* a factor cannot be excluded. Thus, even in the field of diagnostic chest x-rays, it is essential to try to keep exposures to a minimum and to rely more on such old-fashioned methods as physical examination and relatively simple laboratory tests, including the sedimentation rate, the leukocyte count, the relation of monocytes to lymphocytes, etc. In our rapidly advancing civilization, full of hurry and worry, a reversion to even minor degrees of simplicity, although it may smack of being reactionary, may well be desirable.

WILLIAM DAMESHEK, M.D.**

**From the Blood Research Laboratory, a unit of the Ziskind Laboratories, New England Center Hospital, and the Department of Medicine, Tufts University School of Medicine.

Editorial

A Glance at the International Congresses on Diseases of the Chest

During the occasion of my participation in the Pan-American Congress of the ULAST, held at Mexico City in January, 1949, I was approached by the leaders of the American College of Chest Physicians. They requested that I consider the institution and direction of the First International Congress of Chest Physicians, to be held in Rome at the "Carlo Forlanini Institute." This request gave me much inner happiness as I considered it a manifestation of great friendship and an expression of universal solidarity on the part of the American people. The tendering of this invitation by leading medical representatives of that country increased my happiness many-fold.

The great tragedy of the Second World War was not quite over when physicians around the globe began shaking hands again in mutual understanding. As our illustrious colleague, Dr. Arnold S. Anderson, pointed out in his editorial, "Doctors and Peace," written in 1955, the onset of World War II would never have been permitted had the ultimate decision of such tremendous import rested in the hands of physicians, whose eternal enemy is represented by the illnesses and sufferings of mankind.

It was not by mere chance that the Eternal City was selected to be the site of the First International Congress of the American College of Chest Physicians, enabling us to renew those personal contacts so beneficial to the advancement of our knowledge, after a serious and somewhat tearful interruption of our mutual reciprocal relations for a period of 10 years. Nor was it chance alone that many physicians came from distant countries to participate in this Congress, for regardless of their serious inclinations towards medical research, they were not immune to the spell of art and poetry which permeated this eternal city. Also, regardless of personal philosophy and religious belief, they recognized in the universal qualities of humanism, the true flame of life and human progress.

The noble and idealistic tenets of this Congress, in a sense representing the links in a chain, have been successively strengthened by the Congresses which have followed, respectively, in Rio de Janeiro, Barcelona, Cologne, and will extend next year to the Far East, namely Tokyo. This global ramification signifies that no barrier of states, continents, peoples or races exists, but that life in general is sacred and inviolable everywhere it is, and must be protected against the vicissitudes of illness, with its physical and/or moral pain.

In our present realm of scientific knowledge many important contributions have been added to the pathology, pathologic physiology and therapy of chest diseases. We truly are living in a wonderful era, as we note the progress of scientific studies. Bacteriologists, experimental researchers, biochemists, physiologists, thoracic surgeons, bronchoscopists, and cardiologists have seemingly united under one common banner. These individuals have combined and redoubled their efforts for the one main purpose,

i.e., to bring health and happiness to a suffering humanity.

I shall not attempt to point out the principal contributions of the various members of the American College of Chest Physicians, particularly in regard to their theories and practical corollaries thereof, since these would certainly be done by the scientific council which presides over the medical organization of these congresses. I wish only to state that unfading footprints have been marked in the fields of medical and surgical therapy and physiologic mechanics of pulmonary tuberculosis. We may also cite the similar advances made in the infectious pulmonary diseases, in the therapy of the pneumonias, pulmonary emphysema, bronchial asthma, surgical treatments of congenital and acquired heart disease, as well as in the diagnostic and therapeutic consideration of diseases of the esophagus and bronchial tree.

The American College of Chest Physicians can be proud of these results and of the increasing success of its International Congresses. But it would be a great mistake if we reviewed our past accomplishments with a sense of exceeding pride, and thus became blinded to the greater objectives, still unattained, which lie ahead and which can be reached by the younger and more capable students who will be the research men and adherents of our traditions in the future.

We must, therefore, be responsible for the direction and training of their research potentialities as well as kindling within their hearts an enthusiasm for our science of pulmonary disease. The creation of postgraduate courses appears to be directed to this problem and the future results promise to be even greater than that achieved to the present time, thus uniting teachers and pupils of every nation of the world in an indivisible bond. I, therefore, believe that ultimate expansion of these courses is imperative with proper integration and development of the teaching of pathology, physiology, and medical approach to the clinical problem, thus diminishing untoward accentuation of surgical therapy and the relegation of this latter to its proper place in the consideration of thoracic diseases. Thus pathologists, clinicians and surgeons must proceed together, assisting one another, always keeping in mind their common objective, that of healing the sick.

I am sure that in the pursuance of these objectives, the American College of Chest Physicians will be upheld completely in its principal purpose, i.e., to advance the dissemination of scientific knowledge among its members, and to contribute ever increasingly to the benefit and greater happiness of the peoples of the world.

A. OMODEI ZORINI, M.D., F.C.C.P.*

*President, First International Congress on Disease of the Chest, Rome, Italy, Septemper, 1950.

The President's Page

In this message, my first as President of the College, I wish to express my appreciation to the membership for the confidence expressed in electing me to this high office and to assure you that I will attempt to conduct the activities of the College to the best of my ability.

Soon after assuming the presidency, I formulated a questionnaire which was mailed to every member of record. In that questionnaire, I inquired about your special interests in the field of diseases of the chest and if you had some new and original work which you would like to present to the Committee on Scientific Program for the 1958 Annual Meeting of the College to be held in San Francisco. You were also given the opportunity to serve on one of our many important committees. Nearly 1,000 replies have been received; if you did not receive the questionnaire, please let me know and I will send one to you.

Appointments to the College committees are now being made in light of the member's personal interest and the available openings. I would ask those members who received notice of their appointments to mail their acceptances to me promptly and to send a copy to their chairman. This will assist us in getting the activities of the various committees under way with the least possible delay. Each committee will formulate its own program and members will meet in annual session to discuss these programs. It is expected that all committee members will attend the meetings and actively participate in all of the proceedings.

Several important committee reports have been published in our journal during the past few months. I would like to call your attention to the report entitled "Present Status of Chemotherapy in Tuberculosis," by the Committee on Chemotherapy and Antibiotics, the report on "Influenza," by the Council on Public Health, and the "Report of the Committee on Resident Fellowships."

The Council on Postgraduate Medical Education will open the fall season with the 12th Annual Postgraduate Course on Diseases of the Chest to be held in Chicago, October 21-25. This course will be followed by the 10th Annual Postgraduate Course in New York City, November 11-15, and the 3rd Annual Postgraduate Course on Diseases of the Chest to be presented in Los Angeles, December 9-13. It is hoped that many of our members will take advantage of these opportunities to learn about the most recent advances in the specialty of chest disease.

At the 23rd Annual Meeting of the College held in New York City, the Board of Regents authorized the publication of the tenth edition of the College Directory. More than 1,100 new members will be listed in the 1958 Directory. Recently you were sent a proof of your listing and it is hoped that you have returned it to the Executive Offices of the College in Chicago to assure the publication of the correct information.

In this issue of the journal you will find the preliminary program for the Interim Session of the College to be held in Philadelphia on December 2. Dr. Robert V. Cohen and his energetic committee have arranged an excellent scientific session for this meeting and I trust that many of our members are planning to attend. The Clinical Meeting of the American Medical Association will also be held in Philadelphia, December 3-6, which offers another opportunity to hear some excellent papers on diseases of the chest, in addition to viewing the splendid scientific and technical exhibits. The Board of Regents and Board of Governors of the College will meet in Philadelphia on Tuesday, December 3.

May I add a personal word to announce my retirement as President of the Woman's Medical College of Pennsylvania and my recent appointment as Director of Education, Coordinator of Research and Consultant in Cardiopulmonary Physiology at the Lovelace Foundation for Education and Research, Albuquerque, New Mexico. My wife, Margaret, and I will be glad to meet old friends and new who may be passing through the lovely city of Albuquerque. The latchstring is always out.

Burgess L. Gordon

COLLEGE INTERIM SESSION

Warwick Hotel, Philadelphia, December 2, 1957

The scientific program to be presented at the Interim Session of the College, which will be held at the Warwick Hotel, Philadelphia, on Monday, December 2, is nearly complete. The following papers will be presented:

Modern Radiotherapy of Bronchogenic Carcinoma
Milton Friedman, New York City
Discussor: Edgar Mayer, New York City

The Interrelation of Pulmonary and Esophageal Disease
Paul H. Holinger, Chicago, Illinois
Discussor: Arthur M. Olsen, Rochester, Minnesota

Physical Methods of Enhancing the Efficiency of Ventilation in Pulmonary Emphysema
Alvan L. Barach, New York City
Discussor: Albert H. Andrews, Chicago, Illinois

Cytologic Findings in Non-Malignant Chest Diseases
Seymour M. Farber, San Francisco, California
Discussor: Edith E. Sproul, New York City

Traumatic Heart Disease
John S. LaDue, New York City
Discussor: Benjamin Manchester, Washington, D. C.

Surgery in Aortic Valve Disease
Charles A. Hufnagel, Washington, D. C.
Discussor: David H. Waterman, Knoxville, Tennessee

Present Advances in Vascular Surgery
Michael E. DeBakey, Houston, Texas
Discussor: Osler A. Abbott, Emory University, Georgia

Usefulness of Biopsy Techniques in Pulmonary Disease
Laurence K. Groves, Cleveland, Ohio
Discussor: Karl P. Klassen, Columbus, Ohio

Respiratory Problems in the Neonatal Period
Roy F. Goddard, Albuquerque, New Mexico
Discussor: Arthur DeBoer, Chicago, Illinois

Modern Concepts in the Dietary Treatment of Coronary Heart Disease,
Jeremiah Stamler, Chicago, Illinois
Discussor: Abraham Jezer, New York City

The following panel discussions will be presented, one at the end of the morning session and the other in the afternoon session:

The Management of Pulmonary Emphysema
Moderator: R. Drew Miller, Rochester, Minnesota
Panel: Hylan A. Bickerman, New York City
Otto C. Brantigan, Baltimore, Maryland
Harold A. Lyons, Brooklyn, New York

The Evaluation of Cardiac Disability
Moderator: Coleman B. Rabin, New York City
Panel: Irvin Klein, New York City
Norman O. Rothermich, Columbus, Ohio
F. Mason Sones, Jr., Cleveland, Ohio

At noon the following round table luncheon discussions will be held:

Present and Future Developments in Heart Surgery
Egbert H. Fell, Chicago, Illinois; Alfred Goldman, Beverly Hills, California; Dwight E. Harken, Boston, Massachusetts
Moderator: John F. Briggs, St. Paul, Minnesota

Long Term Results of Chemotherapy in Tuberculosis
Sumner S. Cohen, Oak Terrace, Minnesota; Alfred S. Dooneief, Mt. Kisco, New York; Robert Goodwin, Nashville, Tennessee
Moderator: William Tucker, Washington, D. C.

Anticoagulant Therapy in Acute and Chronic Coronary Heart Disease
Henry Russek, Staten Island, New York; Joseph Ryan, St. Paul, Minnesota; Sidney Sherlis, Baltimore, Maryland
Moderator: Simon Dack, New York City

Inhalation Therapy
Gustav J. Beck, New York City; Maurice S. Segal, Boston, Massachusetts; Joseph F. Tomashefski, Columbus, Ohio
Moderator: Edwin R. Levine, Chicago, Illinois

A cocktail party and dinner will be given on Monday evening, to which all College members and their families and guests are invited. The following Fireside Conferences will be held after dinner:

Surgery of the Coronary Arteries
Claude S. Beck, Cleveland, Ohio and Charles B. Ripstein, New York City

Recent Tuberculin Converters
W. Leonard Howard, Northville, Michigan and J. Arthur Myers, Minneapolis, Minnesota

Management of Emphysema
Andrew L. Banyai, Milwaukee, Wisconsin and Herbert C. Sweet, St. Louis, Missouri

Coronary Disease
Arthur Grishman, New York City and Nathaniel E. Reich, Brooklyn, New York

Collagen Diseases Affecting the Lungs
Alvis E. Greer, Houston, Texas and Eli H. Rubin, New York City

Asthma
Bret Ratner, New York City and Leon Unger, Chicago, Illinois

The Place of BCG in the Control of Tuberculosis
Milton I. Levine and George G. Ornstein, New York City

Congestive Heart Failure
Louis F. Bishop, New York City and Paul D. Camp, Richmond, Virginia

Chemotherapy in Pulmonary Disease
Edward Dunner, Washington, D. C. and Alfred Goldman, St. Louis, Missouri

Cor Pulmonale
Robert B. Durham, Atlantic City and Gerard M. Turino, New York City

Bronchiectasis
Daniel C. Baker, Jr., New York City and Arthur C. White, Nashville, Tennessee

Hypertension
Irving Graef, New York City and Maurice A. Schnitker, Toledo, Ohio

Surgery of Lung Tumors
Edgar W. Davis, Washington, D. C. and William L. Watson, New York City

Psychosomatic Aspects of Pulmonary Disease
J. D. Matis, New York City and Emil Rothstein, Brockton, Massachusetts

Dr. Robert V. Cohen, Philadelphia, chairman of the scientific program committee has announced that the complete program will be published in the November issue of *Diseases of the Chest*. Physicians planning to attend the meeting are requested to write directly to the Warwick Hotel for reservations, giving arrival and departure dates. The Clinical Meeting of the American Medical Association will take place in Philadelphia, December 3-6.

The Board of Regents and Board of Governors of the College will hold their semi-annual meetings at the Warwick Hotel on Tuesday, December 3. Examinations for Fellowship in the College will be given on that day and meetings of councils and committees are also being scheduled.

College President Visits New Mexico

Dr. Burgess L. Gordon, President of the American College of Chest Physicians, arrived in Albuquerque, New Mexico, September 3, to take over his new position as Director of Medical Education and Coordinator of Research and Education of the Lovelace Foundation for Medical Education and Research. Pictured above, greeting Dr. Gordon on his arrival at the Albuquerque airport are members of the College: Dr. Roy F. Goddard, President of the medical staff of the Lovelace Clinic and Secretary of the College's Council on Research, Dr. Arthur W. Dahlstrom, Chairman of the College's Committee on Indian Affairs, Dr. Gordon, and Dr. J. E. J. Harris, Governor of the College for New Mexico.

On Friday evening, September 6, the New Mexico Chapter of the American College of Chest Physicians held a dinner in honor of Dr. Gordon at the Wayside Inn, Albuquerque, New Mexico. Speakers included: Dr. Goddard as toastmaster, Drs. J. E. J. Harris and Carl H. Gellenthien, founder members of the College organized 23 years ago in Albuquerque, Dr. Junius Evans, president of the New Mexico Trudeau Society, and Dr. Gordon, who spoke on the growth of the college and accepted the invitation of the New Mexico Chapter to hold the College's 25th anniversary meeting in Albuquerque in 1959.

Following the New Mexico Chapter dinner Dr. Gordon delivered an address entitled "The Evolution of Chronic Pulmonary Disease in Older People" at the Bernalillo County Medical Society meeting, held at the Veterans Hospital in

Albuquerque. The meeting was attended by some 125 Albuquerque doctors and chest physicians from all over the state. Dr. Gordon's move to Albuquerque promises to be a stimulation for the entire state, and especially for Albuquerque, the birthplace of the American College of Chest Physicians.

College Chapter News

PACIFIC NORTHWEST CHAPTER

The annual meeting of the Pacific Northwest Chapter will be held in conjunction with the Pacific Northwest Trudeau Society at the Auditorium of the University of Oregon Medical School, Portland, November 8 and 9. Following is the program:

Friday, November 8

Morning Session

Chairman: Peter J. Galante, Portland, Oregon

8:00 a.m. Clinical-pathological Conference
Discussant: Edward H. Morgan, Seattle, Washington

9:00 a.m. Registration

9:30 a.m. "Current Results in Mass Chest X-ray Survey Programs"
E. Harold Laws, John H. Fountain, Cedric Northrup, Seattle, Washington
"A Two to Nine Year Survey of Chest Surgery for Pulmonary Tuberculosis"
R. F. Lane, Sardis, British Columbia
"Atypical Meningeal Tuberculosis—Three Cases"
G. W. J. Fiddes, Prince Rupert, British Columbia
Discussion of the preceding: Z. Urbanek, Vancouver, British Columbia
"A Consideration of Post-resectional Space Problems"
Fred Jarvis, A. R. Dale, Mark Listerud, Seattle, Washington
"Adrenocortical Steroids in the Treatment of Tuberculosis"
Haskell J. Weinstein, John J. Koler, Seattle, Washington
"Prophylaxis of Tuberculous Meningitis in Children"—First Report of U. S. Public Health Service Study
Edwin L. Kendig, Jr., Richmond, Virginia
Discussion

12:30 p.m. Luncheon

Afternoon Session

Chairman: Warren Smith, Tacoma, Washington

1:30 p.m. "Trends in Research in Pulmonary Physiology"
Loren Carlson, Ph.D., Seattle, Washington
"Chemotherapy of Lung Cancer"
Morton Goodman, Portland, Oregon
"Cobalt 60 in Therapy of Lung Cancer"
Milton Hyman, Portland, Oregon
Discussion
"The Surgical Treatment of Cardiospasm"
Franklin R. Smith, Seattle, Washington
"A New Technic for Surgical Treatment of Funnel Chest"
Roland D. Pinkham, Seattle, Washington
Discussion
"Recent Advances in the Biochemistry of Anaphylaxis and their Clinical Implications"
Charles E. Reed, Corvallis, Oregon
"The Effect of Thoracotomy on the White Blood Cell Count"
Albert R. Allen, Selah, Washington
Discussion

4:30 p.m. Business meeting

6:30 p.m. Social hour—Piluso's Theatre Restaurant

7:30 p.m. Dinner Dance

Saturday, November 9

Morning Session

Chairman: William G. Trapp, Vancouver, British Columbia

9:00 a.m. "Pericardial Tumor Simulating Idiopathic Pericarditis"
J. Thomas Payne, G. G. John, J. T. Wiegenstain, Seattle, Washington

"Radiographic Visualization of the Coronary Arteries"
Louis Frische, Charles T. Dotter, Portland, Oregon

Discussion

"Experiences in Total Surgical Correction of Congenital and Acquired Heart Disease Utilizing the Pump Oxygenator"
K. Alvin Merendino, George I. Thomas, John E. Jesseph, Paul W. Herron, Roy R. Vetto, Loren C. Winterscheid, Seattle, Washington

"Carbohydrate Metabolism of the Isolated Perfused Dog Heart"
John E. Jesseph, Paul W. Herron, Loren G. Winterscheid, K. Alvin Merendino, Seattle, Washington

Discussion—Peter Allen, Peter Ashmore, Vancouver, British Columbia

"Polyvinyl (Ivalon Sponge) Prosthesis for Correction of Mitral Insufficiency"
William R. Rumel, Preston R. Cutler, Salt Lake Sity, Utah

"Mitral Valve Surgery—Transventricular Valvuloplasty and Use of Ivalon Sponge Back"
William S. Conklin, Gordon L. Maurice, Portland, Oregon

Discussion

SOUTHERN CHAPTER

The Southern Chapter of the College comprising the 16 Southern states and the District of Columbia, will hold its annual meeting at the National Hotel, Miami Beach, Florida, November 10 and 11. The meeting will precede the annual meeting of the Southern Medical Association in Miami Beach. The chapter will present the following program:

Sunday, November 10

9:00 a.m. Registration

9:25 a.m. Introductory Remarks—Robert E. Schwartz, Hattiesburg, Mississippi, President, Southern Chapter

Hurst B. Hatch, New Orleans, Louisiana, presiding

"A Novel Approach to the Diagnosis of Pleural Effusion"
A. H. Russakoff, Birmingham, Alabama

"Emphysema as Studied by Micro Radiography"
Charles P. Oderr, New Orleans, Louisiana

"Cancer of the Lung Simulating Other Pulmonary Diseases"
Michael M. Marolla, Nashville, Tennessee

"Bronchial Asthma as a Manifestation of Fibrocystic Disease of the Pancreas"
Roy White, Jr., New Orleans, Louisiana

"Histoplasmosis in Cuba"
Augusto Fernandez Conde, Havana, Cuba

12:00 noon Luncheon and Panel Discussion—"Problems Associated with Surgery of Congenital Cardiac Defects"
Lewis H. Bosher, Jr., Richmond, Virginia; J. Girard Converse, Miami, Florida; Paul T. deCamp, New Orleans, Louisiana; Daniel F. Downing, Philadelphia, Pennsylvania; Ellet H. Drake, Detroit, Michigan

1:55 p.m. DeWitt C. Daughtry, Miami, Florida, presiding
Introduction of Daniel E. Jenkins, Houston, Texas, Second Vice President, Southern Chapter

"A Sub-miniature Intracardiac Manometer for Infants and Adults"
Ellet H. Drake, Detroit, Michigan

"The Place of Surgery in Pulmonary Mycotic Infections"
Timothy Takaro, Oteen, North Carolina

"Unsuspected Bronchogenic Carcinoma"
James W. Pate, Roger E. Campbell, Felix A. Hughes, Memphis, Tennessee

"Coin Lesions of the Lung"
James W. Polk, Carlos Taquechal, Jose A. Cubiles, Mount Vernon, Missouri

"The Tracheal Bronchus"
Burnett Schaff, Coral Gables, Florida

"Surgical Treatment of Pulmonary Emphysema"
William A. Hopkins, M. Bedford Davis, William W. Wansker, Atlanta, Georgia

6:00 p.m. Social hour

Monday, November 11

8:45 a.m. Registration

8:55 a.m. Clarence M. Sharp, Jacksonville, Florida, President, Florida Chapter, presiding

Introduction of Joseph S. Cruise, First Vice President, Southern Chapter

"Hypothermic Anesthesia for Cardiac Surgery—Experimental and Clinical Observations"
W. Sterling Edwards, Birmingham, Alabama

"Unusual Diseases of the Pericardium"
Osler A. Abbott and William E. Van Fleit, Atlanta, Georgia

"Chronic Occlusion of Aortic Arch Branches"
E. Converse Peirce, II, Knoxville, Tennessee

"Topography of the Human Coronary Arteries Considered in Relation to Cardiotomy"
Thomas N. James, New Orleans, Louisiana

Fourth Paul A. Turner Memorial Lecture
"Physio-pathology in Pulmonary Tuberculosis"
John H. McClement, New York, New York

12:00 noon Luncheon and business meeting

2:00 p.m. Daniel E. Jenkins, Houston, Texas, presiding

"Ventilatory Response to Inhaled Carbon Dioxide"
Philip Samet, William H. Bernstein, Hyman Turkewitz, Miami Beach, Florida

"Pulmonary Function in Patients with Rheumatoid Spondylitis"
Louis E. Tolbert, Jr., New Orleans, Louisiana

COLLEGE MEETING IN SPAIN

The First National Meeting of the College in Spain (sponsored by the Barcelona Chapter) will be held in Palma de Mallorca, October 31-November 2, 1957. The following program will be presented:

October 31

Panel Discussion: Bronchopulmonary Suppuration
Etiopathogenesis: S. Almansa de Cara, Malaga
Clinical Aspects: J. Manera Ravira, Palma de Mallorca
Bronchoscopic Diagnosis: A. Castella Escabros, Barcelona
Bacteriology: C. Xalabarder, Barcelona

Medical Treatment: J. Alix Alix, Madrid
Surgical Treatment: Prof. R. R. Lozano, Zaragoza

November 2

The Present Status of Surgery for Mitral Stenosis
E. Garcia Ortiz, Madrid

Panel Discussion: Cor Pulmonale
Etiopathogenesis: V. Sorribes Santamaria, Valencia
Clinical Circulatory Aspects: Sureda Blanes and M. Manera Ravira, Palma de Mallorca
Clinical Respiratory Aspects: J. Sabater Valles, Reus
Treatment: L. Trias de Bes, Barcelona

A social program, including guided tours of the Palma area, has been arranged and the meeting will close with a banquet on November 2. Those wishing to attend the meeting may obtain information by writing to the Secretary of the Barcelona Chapter at Corcega 393, Barcelona, Spain.

MIDDLE EAST CHAPTER

The Third Annual Congress of the Middle East Chapter of the College was held in Bhamdoun, Lebanon, at the Hotel Ambassador, August 9-11, 1957. More than fifty physicians representing Iraq, Jordan, Kuwait, Lebanon and Syria attended. Dr. Jamil Anouty, Director General of the Department of Health of Lebanon, officially opened the meeting, followed by addresses by Dr. Negib Saad, President, Order of Physicians of Lebanon, Prof. Dr. Elias Khoury, the Dean of Chest Physicians in Lebanon and Dr. Edouard Barouky, President of the Middle East Chapter. Dr. Papken S. Mugrditchian, Governor of the College for the Middle East, read a message from Dr. Burgess L. Gordon, President of the College, and spoke on College activities. The scientific program included a symposium on "Bronchial Carcinoma" and a panel discussion on "The Home Treatment of Tuberculosis."

During the business meeting which followed the scientific session, the following officers were elected:

President:	Bechir Azme, Damascus, Syria
Vice-President:	Ahmed Salameh, Kuwait, Persian Gulf
Recording Secretary:	Toufic Al-Awar, Bhannes, Lebanon
Corresponding Secretary:	Wagih K. Sabbagh, Beit Mery, Lebanon (Re-elected)

The Fourth Annual Congress of the Chapter will be held in Lebanon in 1958.

ANNOUNCEMENT

The American Trudeau Society will provide a limited number of fellowships to candidates holding the degree of M.D., Ph.D., or Sc.D. to promote the training of clinicians, medical teachers, and scientific investigators in the field of tuberculosis and respiratory diseases. Awards are open to citizens of the United States only.

Residencies in an approval hospital under such a fellowship will be credited by the American Board of Internal Medicine towards certification in internal medicine and pulmonary disease. Predoctoral fellowships are also offered to graduate students who hold a bachelor's degree and are working on a research project for an advanced degree other than M.D.

Each applicant must have the approval of the head of the department under whom he expects to work. All awards are determined by individual circumstances and are paid directly to the fellow on a quarterly basis. Fellowships are granted for one year and fellowship applications must be received by January 1.

A few fellowships at a higher level of training and award are offered to specially qualified candidates with an M.D. degree.

Further particulars concerning fellowships may be obtained from the Director of Medical Education, American Trudeau Society, c/o The Henry Phipps Institute, Seventh and Lombard Streets, Philadelphia 47, Pennsylvania.

CALENDAR OF EVENTS

NATIONAL AND INTERNATIONAL MEETINGS

Interim Session and Semi-Annual Meetings
Board of Regents and Board of Governors
American College of Chest Physicians
Warwick Hotel, Philadelphia, December 2-3, 1957

24th Annual Meeting, American College of Chest Physicians
Fairmont Hotel, San Francisco, June 18-22, 1958

Fifth International Congress on Diseases of the Chest
Council on International Affairs
American College of Chest Physicians
Tokyo, Japan, September 7-11, 1958

POSTGRADUATE COURSES

12th Annual Postgraduate Course on Diseases of the Chest
Hotel Knickerbocker, Chicago, October 21-25

10th Annual Postgraduate Course on Diseases of the Chest
Park-Sheraton Hotel, New York City, November 11-15

3rd Annual Postgraduate Course on Diseases of the Chest
Ambassador Hotel, Los Angeles, December 9-13

11th Annual Postgraduate Course on Diseases of the Chest
Warwick Hotel, Philadelphia, March 3-7, 1958

CHAPTER MEETINGS

New Jersey Chapter, Trenton, October 15

Potomac Chapter, Baltimore, October 20

Virginia Chapter, Washington, D. C., October 27

Pacific Northwest Chapter, Portland, Oregon, November 8-9

Southern Chapter, Miami Beach, Florida, November 10-11

1958 DIRECTORY LISTINGS

If you have not as yet returned your proof for your listing in the 1958 Directory of the College, please do so at once. Members may purchase copies of the 1958 College Directory by ordering immediately at the pre-publication price of $5.00. After publication the price will be $7.50.

MEDICAL SERVICE BUREAU

POSITIONS WANTED

Chest physician, F.C.C.P., Ohio-New York licenses, now assistant medical director, tuberculosis sanatorium, seeks responsible position (directorship, assistant directorship, head of department or clinic, etc.). Also will consider part-time position permitting part-time private practice. Please address inquiries to Box 292B, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

British graduate, F.C.C.P., age 43, holding Canadian medical license, seeks permanent hospital or sanatorium appointment in Canada or United States. Extensive clinical and teaching experience in sanatoria and specialist chest hospitals. References. Please address inquiries to Box 293B, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Tuberculosis specialist, age 44, F.C.C.P., now chief of 336-bed tuberculosis service, would like to work in a sanatorium in the general area of New York City or New Jersey for 6 months. Please address inquiries to Box 294B, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illniois.

Chest physician, F.C.C.P., graduate of approved American school, 16 years' experience in diseases of the chest, age 43, married, presently medical director and superintendent of 110-bed tuberculosis hospital, seeks similar position in the south or southwest. Please address inquiries to Box 295B, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

POSITIONS AVAILABLE

Board eligible internist wanted for Florida State Tuberculosis Hospitals. Rapidly developing program with opportunities for advancement. Beautiful hospitals. Furnished houses available. Liberal retirement and other benefits. Salary dependent upon qualifications. Write: Roberts Davies, M.D., Director, State Tuberculosis Board, P.O. Box 286, Tallahassee, Florida.

Staff physician wanted for 215-bed hospital for chronic pulmonary diseases. Salary commensurate with qualifications and experience. Living quarters and laundry are provided. Must be a graduate of an approval school. Contact E. W. Hainlen, M.D., Director of Medical Services, Emily P. Bissell Sanatorium, 3000 Newport Gap Pike, Wilmington 8, Delaware.

Associate physician wanted for approved chest disease hospital to assist in supervision of patient care. Must be eligible for California license. Salary $9,600 to $10,000 per annum start. Please address inquiries to Box 292A, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Assistant physician wanted for tuberculosis hospital. Must be eligible for California license. Salary $8400 per annum. Please address inquiries to Box 293A, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Resident surgeon wanted for 500-bed tuberculosis hospital with active thoracic surgery department. Apply giving details of training to: Medical Director, Southeast Florida Tuberculosis Hospital, Box 1411, Lantana, Florida.

Phone: Clayburn 8-4921

Direct all communications to:
B. H. Wardrip, M.D.
Medical Director
P.O. Box 71
San Jose, California

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Section for General Medicine
Section for Diseases of the Chest

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100 Beds for Crippled Children — *200 Beds for Tuberculosis*

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Medical Director
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For The

FIFTH INTERNATIONAL CONGRESS ON DISEASES OF THE CHEST

Sponsored by the Council on International Affairs
American College of Chest Physicians

Presented under the Patronage of the
Government of Japan

TOKYO, JAPAN **SEPTEMBER 7-11, 1958**

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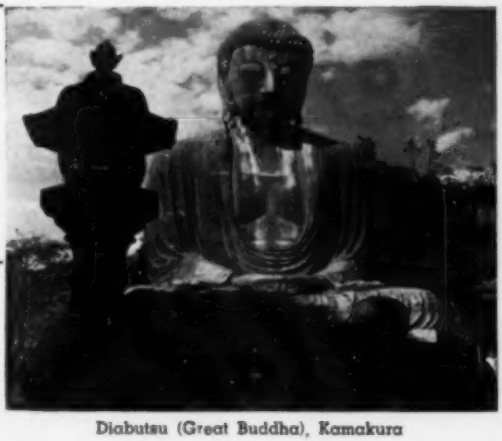

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Upon completion of arrangements for the tours, a printed brochure containing all pertinent information will be made available this fall by Cartan Travel Bureau, Inc., Chicago, official travel agency for the Congress.

For further information please write to the Executive Director, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois

THE EDITORIAL BOARD

FOR

DISEASES OF THE CHEST

is pleased to announce . . .

SECTION ON CARDIOVASCULAR DISEASES

to be published in each issue of the College Journal

DISEASES OF THE CHEST

effective

JANUARY, 1958

This new Section is being established because of the growth of the College and the varied interests of its members. The new Section will facilitate the selection of scientific papers of significance to our readers. The Editorial Board welcomes recommendations at all times relative to the improvement and maintenance of the high standards of the Journal.

J. Arthur Myers, M.D.
Editor-in-Chief

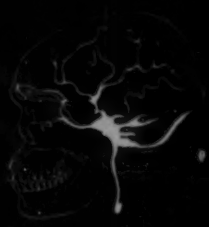
AP and lateral thorax radiography

Using Camera A or B

Silicosis research and bronchography

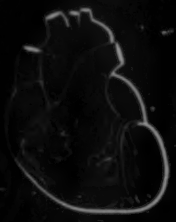
Using Camera A or B

Cerebral angiography



Using Camera A or C

Angiocardiography, angiography



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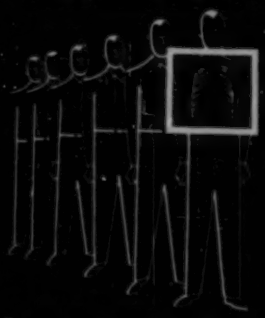
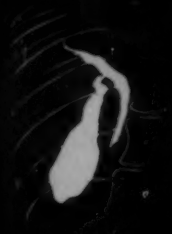
Mass chest survey



Using Camera A or B

G. I., kidneys and gall-bladder radiography



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For more details, contact your X-ray equipment dealer, or write to: Fairchild Camera and Instrument Corporation, Industrial Camera Division, 5 Aerial Way, Syosset, New York, Dept. 160-51R.

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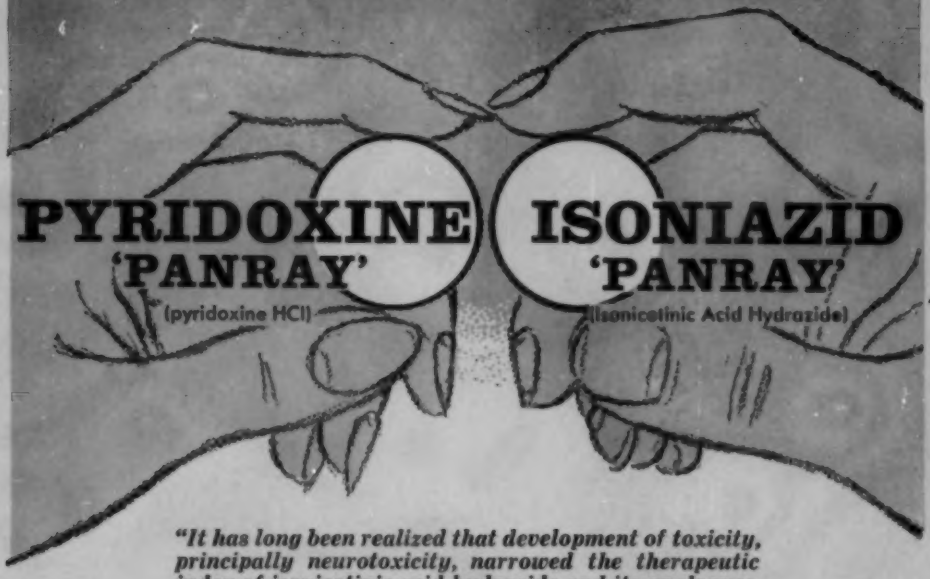

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[1]See View Bulletin 16:62 July '56 Tchertkoff, et al. JAMA 156:1549 (Dec. 25) 1954 Biehl & Vilmer Am. Rev. Tbc 70:266 Aug. '54 Hughes, et al. N. Eng. J. of Med. 255 #3 118-122, 1956 Carlson, et al.